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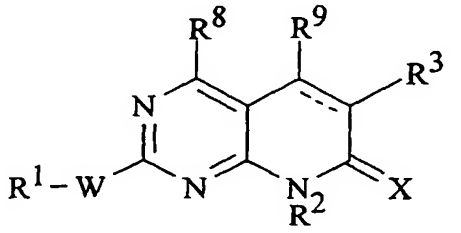
(54) Title: PYRIDOPYRIMIDINONE DERIVATIVES FOR TREATMENT OF NEURODEGENERATIVE DISEASE



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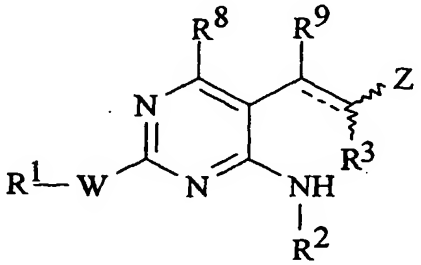

(II)

(57) Abstract: This invention provides a method for treating neurodegenerative diseases in mammals comprising administering an effective amount of a cyclin-dependent kinase inhibitor. A preferred method uses cdk inhibitors of Formula (I) and Formula (II) where W is NH, S, SO, or SO_2, R^1 includes phenyl and substituted phenyl, R^2 includes alkyl and cycloalkyl, R^3 includes alkyl and hydrogen, R^8 and R^9 include hydrogen and alkyl, and Z is carboxy.

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PYRIDOPYRIMIDINONE DERIVATIVES FOR TREATMENT OF NEURODEGENERATIVE DISEASE

FIELD OF THE INVENTION

This invention concerns a method of treating neurodegenerative diseases in mammals by administering compounds that inhibit cyclin-dependent kinase enzymes. The invention also provides novel compounds that are useful in the method.

BACKGROUND OF THE INVENTION

Neurodegenerative diseases are conditions characterized by breakdown and dysfunction of neuronal activity. Diseases commonly falling within the neurodegenerative term include Alzheimer's disease (AD), Huntington's disease, Parkinson's disease, and Amyotrophic Lateral Sclerosis. Other conditions which result from degeneration of neuronal function are progressive supernuclear palsy (PSP) and pronto-temporal dementia linked to Parkinson's disease (FTDP-17).

Neurodegenerative diseases often accompany the aging process, and these diseases are becoming more prevalent throughout the world as the general population reaches about 60 years of age and older. Even though neurodegenerative diseases have afflicted mankind for many years, the underlying causes remain unknown, and there are no cures. Several agents are available for treating the symptoms and physical effects of these diseases, but most are only marginally effective. The need continues to find new and better agents for treating these debilitating diseases.

We have now discovered that compounds that inhibit certain enzymes called cyclin-dependent kinases (cdks) are useful for treating neurodegenerative diseases. Cyclin-dependent kinases are cellular enzymes that perform essential functions in regulating cell division and proliferation. The cyclin-dependent kinase catalytic units, of which 9 have now been described, are activated by regulatory subunits known as cyclins. At least 16 mammalian cyclins have been identified, including cyclin B/cdk1, cyclin A/cdk2, cyclin E/cdk3, cyclin D/cdk4, and the neuronal cdk2-like kinase known as cdk5. Cdk5, together with its brain-specific activator protein known as p35/p25, promotes phosphorylation of

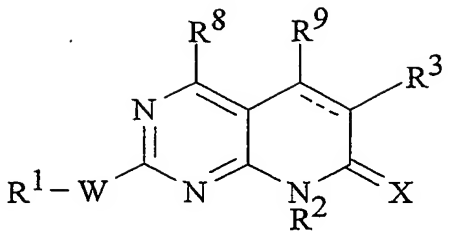
the neuron-specific microtubule-associated protein known as tau (Lew, et al., *Trends Biochem. Sci.*, 1995;20:33-37). Aberrant expression of cdk5 contributes to the neurodegenerative disorder multiple system atrophy (Nakamura, et al., *J. Neuropathol. Exp. Neurol.*, 1998;57:690). The tau protein has long been associated with hyperphosphorylation in the pathogenesis of AD (Spillantini, et al), *Trends Neurosci.*, 1998;21:428-433). In addition to amyloid plaques, neurofibrillary tangles are a primary marker for AD, and the major component of these neurofibrillary tangles is a substance known as paired helical filament-tau. This is a filamentous aggregate of hyperphosphorylated tau. Abnormal activation of protein kinase enzymes, and especially cyclin-dependent kinase 5 (cdk5) promotes tau hyperphosphorylation, and pathological activation of cdk5 appears to be a major contributor to the formation of hyperphosphorylated-tau.

We have thus found that compounds which inhibit cyclin-dependent kinases, and especially cdk5, are useful in treating neurodegenerative diseases. An object of this invention is to provide a method for treating neurodegenerative disease in mammals comprising administering an effective amount of a cdk inhibitor.

SUMMARY OF THE INVENTION

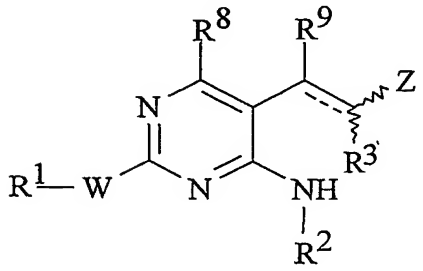
This invention is a method for treating neurodegenerative diseases in mammals comprising administering an effective amount of an inhibitor of a cyclin-dependent kinase enzyme. In a preferred embodiment, the cdk inhibitor is a compound that inhibits cdk5 more than any of the other cdk enzymes. Any cdk inhibitor will work in the method of this invention, provided it inhibits cdk5 to some extent.

In a preferred embodiment, the compound to be administered according to this invention is a pyridopyrimidine or aminopyrimidine cdk inhibitor. Such compounds are disclosed in WO 98/33798, US Patents 5,952,342 and 5,733,913, all incorporated herein by reference. Especially preferred cdk inhibitors are pyrido[2,3-d]pyrimidines and 4-aminopyrimidines of Formulas I and II below:



I

and



II

wherein:

W is NH, S, SO, or SO_2;

R^1 and R^2 include alkyl, cycloalkyl, substituted alkyl, substituted cycloalkyl, aryl, and heteroaryl;

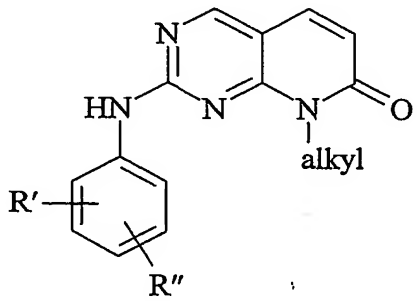
R^3 includes hydrogen, alkyl, and halogen;

X is O, S, or NH;

R^8 and R^9 independently are hydrogen, alkyl, alkoxy, halo, amino, and the like;

and pharmaceutically acceptable salts thereof.

An especially preferred method of this invention comprises administering a compound of Formula III:



III

where alkyl is straight or branched C_1-C_6 alkyl, and R′ and R″ independently are hydrogen, hydroxy, halo, nitro, or C_1-C_6 alkoxy.

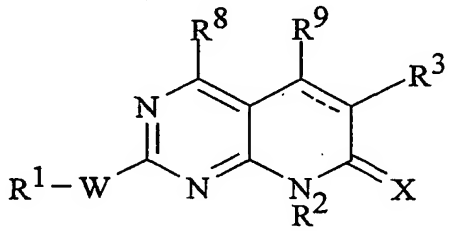
In another preferred embodiment, the foregoing compounds are used to treat neurodegenerative diseases selected from Alzheimer's, Huntington's, and Parkinson's diseases.

DETAILED DESCRIPTION OF THE INVENTION

All that is required to practice the method of treating neurodegenerative disease according to this invention is to administer to a mammal who is suffering from a neurodegenerative disease and in need of treatment, an effective amount of a cdk inhibitor having cdk5 inhibitory activity.

As used herein, a "cdk inhibitor" is any compound that inhibits at least fifty percent (50%) of at least one cdk enzyme at a concentration (IC_{50}) of at least 5000 nanomolar (nM) when evaluated in a standard cyclin-dependent kinase assay. Preferably, the cdk inhibitors to be administered according to this invention will exhibit an IC_{50} against cdk5 of at least 500 nM.

Preferred cdk inhibitors to be used in this invention are defined by Formula I:



I

and the pharmaceutically acceptable salts thereof,

wherein:

the dotted line represents an optional double bond;

W is NH, S, SO, or SO_2;

X is either O, S, or NH;

R^1 and R^2 are independently selected from the group consisting of H, $(CH_2)_nAr$, $(CH_2)_n$heteroaryl, $(CH_2)_n$heterocyclyl, C_1-C_{10} alkyl, C_3-C_{10} cycloalkyl, C_2-C_{10} alkenyl, and C_2-C_{10} alkynyl, wherein n is 0, 1, 2, or 3, and the $(CH_2)_nAr$, $(CH_2)_n$heteroaryl, alkyl, cycloalkyl, alkenyl, and alkynyl groups are optionally substituted by up to 5 groups selected from NR^4R^5,

$N(O)R^4R^5$, $NR^4R^5R^6Y$, alkyl, phenyl, substituted phenyl, $(CH_2)_n$heteroaryl, hydroxy, alkoxy, phenoxy, thiol, thioalkyl, halo, COR^4, CO_2R^4, $CONR^4R^5$, $SO_2NR^4R^5$, SO_3R^4, PO_3R^4, aldehyde, nitrile, nitro, heteroaryloxy, $T(CH_2)_mQR^4$, $T(CH_2)_mC(OR^5)H-(CH_2)_mQR^4$, $C(O)T(CH_2)_mQR^4$, $NHC(O)T(CH_2)_mQR^4$, $T(CH_2)_mC(O)NR^4NR^5$, or $T(CH_2)_mCO_2R^4$ wherein each m is independently 1-6, T is O, S, NR^4, $N(O)R^4$, NR^4R^6Y, or CR^4R^5, and Q is O, S, NR^5, $N(O)R^5$, or NR^5R^6Y;

R^3 is H, alkyl, halogen, NO_2, NR^4R^5, $COOR^4$, OR^4, CN, or $CONR^4R^5$;

R^4 and R^5 are each independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, substituted alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, $(CH_2)_n$Ar, C_3-C_{10} cycloalkyl, heterocyclyl, and heteroaryl, or R^4 and R^5 together with the nitrogen to which they are attached optionally form a ring having 3 to 7 carbon atoms and said ring optionally contains 1, 2, or 3 heteroatoms selected from the group consisting of nitrogen, substituted nitrogen, oxygen, and sulfur;

When R^4 and R^5 together with the nitrogen to which they are attached form a ring, the said ring is optionally substituted by 1 to 3 groups selected from OH, OR^4, NR^4R^5, $(CH_2)_mOR^4$, $(CH_2)_mNR^4R^5$, $T\text{-}(CH_2)_mQR_4$, $CO\text{-}T\text{-}(CH_2)_mQR^4$, $NH(CO)T(CH_2)_mQR^4$, $T\text{-}(CH_2)_mCO_2R^4$, or $T(CH_2)_mCONR^4R^5$;

R^6 is alkyl;

R^8 and R^9 independently are H, C_1-C_3alkyl, NR^4R^5, $N(O)R^4R^5$, $NR^4R^5R^6Y$, hydroxy, alkoxy, thiol, thioalkyl, halo, COR^4, CO_2R^4, $CONR^4R^5$, $SO_2NR^4R^5$, SO_3R^4, PO_3R^4, CHO, CN, or NO_2; and

Y is a halo counter-ion.

An especially preferred group of compounds of Formula I have the above formula wherein X is O.

Another preferred group of compounds are those wherein W is NH.

A preferred group of compounds of Formula I have the above formula wherein X is O, and R^3 is CH_3 or H. In an especially preferred group of compounds, X is O, and R^3 is H.

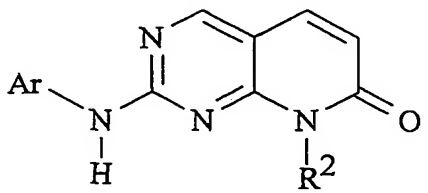
Also preferred are compounds of Formula I wherein R^8 and R^9 both are hydrogen.

Another preferred group of compounds of Formula I have the above formula wherein X is O, and R^2 is Et, Pr, *i*-Pr, *i*-Bu, *i*-pentyl, or cycloalkyl. In an especially preferred group of compounds, X is O and R^2 is *i*-Pr or *i*-pentyl.

In yet another preferred group of compounds of Formula I, X is O, and R^1 is phenyl. Another preferred group of compounds of Formula I have one or more of the following structural features: X is O, and there is a double bond between C_5 and C_6, R^1 is phenyl, optionally substituted with 4-piperidinyl (with or without substitution), 4-(2-diethylaminoethoxy) or 4-(4-methyl piperazin-1-yl); and R^2 is a branched alkyl or cycloalkyl, including but not limited to isopropyl, cyclopentyl, cyclohexyl, or norbornyl. In an especially preferred group of compounds, X is O, and R^1 is phenyl substituted with hydroxy, alkoxy, NR^4R^5, or $T(CH_2)_mQR^4$, where R^4 and R^5, T, m, and Q all are as defined above. In an even more preferred group of compounds, X is O, and R^1 is phenyl substituted with NR^4R^5 or $T(CH_2)_mQR^4$, where R^4 and R^5, T, m, and Q all are as defined above.

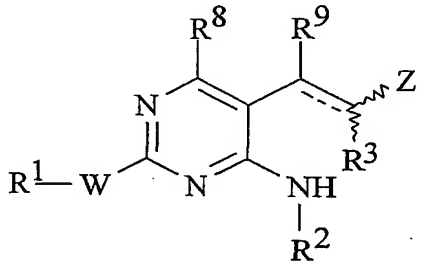
Another preferred group of compounds of Formula I are those wherein X is NH.

The most preferred compounds of the present invention have the formula:



where R^2 is as defined above, and Ar is phenyl, substituted phenyl, or heteroaryl. Ideally, R^2 is alkyl such as ethyl, isopropyl, propyl, butyl, or isopentyl, or cycloalkyl such as norbornyl, cyclohexyl, or adamantyl. A most preferred Ar group is phenyl, preferably substituted with 1, 2, or 3 groups selected from phenyl, chloro, bromo, fluoro, methyl, methoxy, hydroxy, hydroxymethyl, 2-diethylaminoethoxy, methoxycarbonylmethyl, carboxy, carboxymethyl, ethoxycarbonyl, nitro, 2-carboxyethyl, 2-ethoxycarbonylethyl, NR^4R^5, and $O(CH_2)_{0-6}NR^4R^5$, wherein R^4 and R5 are as defined above. Another preferred Ar group is thiazolyl, for example, 2-thiazolyl, optionally substituted by phenyl, hydroxyphenyl, or alkoxyphenyl.

Another group of cdk inhibitors useful in the method of this invention are those of Formula II:



II

wherein:

the dotted line represents an optional double bond of either trans or *cis*-stereochemistry;

W is NH, S, SO, or SO_2;

Z is $COOR^7$, CN, CHO, CH_2OR^7, CH_2NHR^7, $CONHR^7$, or COR^7;

R^1 and R^2 are independently selected from the group consisting of H, $(CH_2)_nPh$, $(CH_2)_n$heteroaryl, $(CH_2)_n$heterocycle, C_1-C_{10} alkyl, C_3-C_{10} cycloalkyl, C_2-C_{10} alkenyl, and C_2-C_{10} alkynyl, wherein n is 0, 1, 2, or 3 and the $(CH_2)_nPh$, $(CH_2)_n$heteroaryl, alkyl, cycloalkyl, alkenyl, and alkynyl groups are optionally substituted by groups of NR^4R^5, $N(O)R^4R^5$, $NR^4R^5R^6Y$, phenyl, substituted phenyl, hydroxy, alkoxy, phenoxy, thiol, thioalkyl, halo, COR^4, CO_2R^4, $CONR^4R^5$, $SO_2NR^4R^5$, SO_3R^4, PO_3R^4,

aldehyde, nitrile, nitro, heteroaryloxy, $T(CH_2)_mQR^4$, $C(O)T(CH_2)_mQR^4$, $NHC(O)T(CH_2)_mQR^4$, or $T(CH_2)_mCO_2R^4$ wherein m is 1 to 6, T is O, S, NR^4, $N(O)R^4$, NR^4R^6Y, or CR^4R^5, and Q is O, S, NR^5, $N(O)R^5$, or NR^5R^6Y;

R^3 is H or alkyl;

R^4 and R^5 are independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, substituted alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, $(CH_2)_nPh$, C_3-C_{10} cycloalkyl, and heteroaryl, or R^4 and R^5 together with the nitrogen to which they are attached optionally form a ring having 3 to 7 carbon atoms and said ring optionally contains 1, 2, or 3 heteroatoms selected from the group consisting of nitrogen, substituted nitrogen, oxygen, and sulfur;

R^6 is alkyl;

Y is a halo counter-ion;

R^7 is one of H, lower alkyl, or phenyl.

R^8 and R^9 independently are H, C_1-C_3alkyl, NR^4R^5, $N(O)R^4R^5$, $NR^4R^5R^6$8, hydroxy, alkoxy, thiol, thioalkyl, halo, COR^4, CO_2R^4, $CONR^4R^5$, $SO_2NR^4R^5$, SO_3R^4, PO_3R^4, CHO, CN, or NO_2;

and the pharmaceutically acceptable salts thereof.

Preferably, compounds of Formula II have a trans double bond between C_5 and C_6, more preferably with R^1 being phenyl, and even more preferably with both R^1 being phenyl and R^2 being alkyl or cycloalkyl.

Also preferred are compounds of Formula II wherein R^8 and R^9 both are hydrogen.

Examples of NR^4R^5 groups include amino, methylamino, di-isopropylamino, acetyl amino, propionyl amino, 3-aminopropyl amino, 3-ethylaminobutyl amino, 3-di-n-propylamino-propyl amino, 4-diethylaminobutyl amino, and 3-carboxypropionyl amino. R^4 and R^5 can be taken together with the nitrogen to which they are attached to form a ring having 3 to 7 carbon atoms and

1, 2, or 3 heteroatoms selected from the group consisting of nitrogen, substituted nitrogen, oxygen, and sulfur. Examples of such cyclic NR^4R^5 groups include pyrrolidinyl, piperazinyl, 4-methylpiperazinyl, 4-benzylpiperazinyl, pyridinyl, piperidinyl, pyrazinal, morpholinyl, and the like.

Unless otherwise expressly stated, the following definitions are adhered to throughout this disclosure.

"Alkyl" means a straight or branched hydrocarbon radical having from 1 to 10 carbon atoms (unless stated otherwise) and includes, for example, methyl, ethyl, n-propyl, isopropyl, n-butyl, sec-butyl, isobutyl, tert-butyl, n-pentyl, iso-pentyl, n-hexyl, and the like.

"Halo" includes fluoro, chloro, bromo, and iodo.

"Alkenyl" means straight and branched hydrocarbon radicals having from 2 to 6 carbon atoms and one double bond and includes ethenyl, 3-buten-1-yl, 2-ethenylbutyl, 3-hexen-1-yl, and the like.

"Alkynyl" means straight and branched hydrocarbon radicals having from 2 to 6 carbon atoms and one triple bond and includes ethynyl, 3-butyn-1-yl, propynyl, 2-butyn-1-yl, 3-pentyn-1-yl, and the like.

"Cycloalkyl" means a monocyclic or polycyclic hydrocarbyl group such as cyclopropyl, cycloheptyl, cyclooctyl, cyclodecyl, cyclobutyl, adamantyl, norpinanyl, decalinyl, norbornyl, cyclohexyl, and cyclopentyl. Such groups can be substituted with groups such as hydroxy, keto, and the like. Also included are rings in which 1 to 3 heteroatoms replace carbons. Such groups are termed "heterocyclyl," which means a cycloalkyl group also bearing at least one heteroatom selected from O, S, or NR_2, examples being oxiranyl, pyrrolidinyl, piperidyl, tetrahydropyran, and morpholine.

"Alkoxy" refers to the alkyl groups mentioned above bound through oxygen, examples of which include methoxy, ethoxy, isopropoxy, *tert*-butoxy, and the like. In addition, alkoxy refers to polyethers such as $-O-(CH_2)_2-O-OH_3$, and the like.

"Alkanoyl" groups are alkyl linked through a carbonyl, ie, $C_1-C_5-C(O)-$. Such groups include formyl, acetyl, propionyl, butyryl, and isobutyryl.

"Acyl" means an alkyl or aryl (Ar) group bonded through a carbonyl group, ie, R-C(O)-. For example, acyl includes a C_1-C_6 alkanoyl, including substituted alkanoyl, wherein the alkyl portion can be substituted by NR^4R^5 or a carboxylic or heterocyclic group. Typical acyl groups include acetyl, benzoyl, and the like.

The alkyl, alkenyl, alkoxy, and alkynyl groups described above are optionally substituted, preferably by 1 to 3 groups selected from NR^4R^5, phenyl, substituted phenyl, thio C_1-C_6 alkyl, C_1-C_6 alkoxy, hydroxy, carboxy, C_1-C_6 alkoxycarbonyl, halo, nitrile, cycloalkyl, and a 5- or 6-membered carbocyclic ring or heterocyclic ring having 1 or 2 heteroatoms selected from nitrogen, substituted nitrogen, oxygen, and sulfur. "Substituted nitrogen" means nitrogen bearing C_1-C_6 alkyl or $(CH_2)_nPh$ where n is 1, 2, or 3. Perhalo and polyhalo substitution is also embraced.

Examples of substituted alkyl groups include 2-aminoethyl, pentachloroethyl, trifluoromethyl, 2-diethylaminoethyl, 2-dimethylaminopropyl, ethoxycarbonylmethyl, 3-phenylbutyl, methanylsulfanylmethyl, methoxymethyl, 3-hydroxypentyl, 2-carboxybutyl, 4-chlorobutyl, 3-cyclopropylpropyl, pentafluoroethyl, 3-morpholinopropyl, piperazinylmethyl, and 2-(4-methylpiperazinyl)ethyl.

Examples of substituted alkynyl groups include 2-methoxyethynyl, 2-ethylsulfanyethynyl, 4-(1-piperazinyl)-3-(butynyl), 3-phenyl-5-hexynyl, 3-diethylamino-3-butynyl, 4-chloro-3-butynyl, 4-cyclobutyl-4-hexenyl, and the like.

Typical substituted alkoxy groups include aminomethoxy, trifluoromethoxy, 2-diethylaminoethoxy, 2-ethoxycarbonylethoxy, 3-hydroxypropoxy, 6-carboxhexyloxy, and the like.

Further, examples of substituted alkyl, alkenyl, and alkynyl groups include dimethylaminomethyl, carboxymethyl, 4-dimethylamino-3-buten-1-yl, 5-ethylmethylamino-3-pentyn-1-yl, 4-morpholinobutyl, 4-tetrahydropyrinidylbutyl, 3-imidazolidin-1-ylpropyl, 4-tetrahydrothiazol-3-yl-butyl, phenylmethyl, 3-chlorophenylmethyl, and the like.

The terms "Ar" and "aryl" refer to unsubstituted and substituted aromatic groups. Heteroaryl groups have from 4 to 9 ring atoms, from 1 to 4 of which are independently selected from the group consisting of O, S, and N. Preferred heteroaryl groups have 1 or 2 heteroatoms in a 5- or 6-membered aromatic ring. Mono and bicyclic aromatic ring systems are included in the definition of aryl and heteroaryl. Typical aryl and heteroaryl groups include phenyl, 3-chlorophenyl, 2,6-dibromophenyl, pyridyl, 3-methylpyridyl, benzothienyl, 2,4,6-tribromophenyl, morpholinyl, indolyl, benzotriazolyl, indazolyl, 4-ethylbenzothienyl, furanyl, 3,4-diethylfuranyl, naphthyl, 4,7-dichloronaphthyl, pyrrole, pyrazole, imidazole, thiazole, and the like.

Preferred Ar groups are phenyl and phenyl substituted by 1, 2, or 3 groups independently selected from the group consisting of alkyl, alkoxy, thio, thioalkyl, halo, hydroxy, $-COOR^7$, trifluoromethyl, nitro, amino of the formula $-NR^4R^5$, and $T(CH_2)_mQR^4$ or $T(CH_2)_mCO_2R^4$ wherein m is 1 to 6, T is O, S, NR^4, $N(O)R^4$, NR^4R^6Y, or CR^4R^5, Q is O, S, NR^5, $N(O)R^5$, or NR^5R^6Y wherein R^4 and R^5 are as described above, and R^7 is alkyl or substituted alkyl, for example, methyl, trichloroethyl, diphenylmethyl, and the like. The alkyl and alkoxy groups can be substituted as defined above. For example, typical groups are carboxyalkyl, alkoxycarbonylalkyl, hydroxyalkyl, hydroxyalkoxy, and alkoxyalkyl.

The compounds to be used in the present invention can exist in unsolvated forms as well as solvated forms, including hydrated forms. In general, the solvated forms, including hydrated forms, are equivalent to unsolvated forms and are intended to be encompassed within the scope of the present invention.

The compounds of Formula I and II are capable of further forming both pharmaceutically acceptable formulations comprising salts, including but not limited to acid addition and/or base salts, solvents and N-oxides of a compound of Formula I and/or II. This invention also provides pharmaceutical formulations comprising a compound of Formula I and/or II together with a pharmaceutically acceptable carrier, diluent, or excipient therefor. All of these forms can be used in the method of the present invention.

Pharmaceutically acceptable acid addition salts of the compounds of Formula I and II include salts derived form inorganic acids such as hydrochloric, nitric, phosphoric, sulfuric, hydrobromic, hydriodic, phosphorus, and the like, as well as the salts derived from organic acids, such as aliphatic mono- and dicarboxylic acids, phenyl-substituted alkanoic acids, hydroxy alkanoic acids, alkanedioic acids, aromatic acids, aliphatic and aromatic sulfonic acids, etc. Such salts thus include sulfate, pyrosulfate, bisulfate, sulfite, bisulfite, nitrate, phosphate, monohydrogenphosphate, dihydrogenphosphate, metaphosphate, pyrophosphate, chloride, bromide, iodide, acetate, propionate, caprylate, isobutyrate, oxalate, malonate, succinate, suberate, sebacate, fumarate, maleate, mandelate, benzoate, chlorobenzoate, methylbenzoate, dinitrobenzoate, phthalate, benzenesulfonate, toluenesulfonate, phenylacetate, citrate, lactate, maleate, tartrate, methanesulfonate, and the like. Also contemplated are the salts of amino acids such as arginate, gluconate, galacturonate, and the like; see, for example, Berge, et al., "Pharmaceutical Salts," *J. of Pharmaceutical Science*, 1977;66:1-19.

The acid addition salts of the basic compounds are prepared by contacting the free base form with a sufficient amount of the desired acid to produce the salt in the conventional manner. The free base form may be regenerated by contacting the salt form with a base and isolating the free base in the conventional manner. The free base forms differ from their respective salt forms somewhat in certain physical properties such as solubility in polar solvents, but otherwise the salts are equivalent to their respective free base for purposes of the present invention.

Pharmaceutically acceptable base addition salts are formed with metals or amines, such as alkali and alkaline earth metal hydroxides, or of organic amines. Examples of metals used as cations are sodium, potassium, magnesium, calcium, and the like. Examples of suitable amines are N,N′-dibenzylethylenediamine, chloroprocaine, choline, diethanolamine, ethylenediamine, N-methylglucamine, and procaine; see, for example, Berge, et al., supra.

The base addition salts of acidic compounds are prepared by contacting the free acid form with a sufficient amount of the desired base to produce the salt in the conventional manner. The free acid form may be regenerated by contacting the salt form with an acid and isolating the free acid in a conventional manner. The

free acid forms differ from their respective salt forms somewhat in certain physical properties such as solubility in polar solvents, but otherwise the salts are equivalent to their respective free acid for purposes of the present invention.

The compounds of the present invention can be formulated and administered in a wide variety of oral and parenteral dosage forms, including transdermal and rectal administration. All that is required is that a cdk inhibitor be administered to a mammal suffering from a neurodegenerative disease in an effective amount, which is that amount required to cause an improvement in the neurodegenerative disease and/or the symptoms associated with such disease. It will be recognized to those skilled in the art that the following dosage forms may comprise as the active component, either a compound of Formula I and/or II or a corresponding pharmaceutically acceptable salt or solvate of a compound of Formula I and/or II.

For preparing pharmaceutical compositions with the cdk compounds, pharmaceutically acceptable carriers can be either a solid or liquid. Solid form preparations include powders, tablets, pills, capsules, cachets, suppositories, and dispensable granules. A solid carrier can be one or more substances which may also act as diluents, flavoring agents, binders, preservatives, tablet disintegrating agents, or an encapsulating material.

In powders, the carrier is a finely divided solid such as talc or starch which is in a mixture with the finely divided active component. In tablets, the active component is mixed with the carrier having the necessary binding properties in suitable proportions and compacted in the shape and size desired.

The formulations of this invention preferably contain from about 5% to about 70% or more of the active compound. Suitable carriers include magnesium carbonate, magnesium stearate, talc, sugar, lactose, pectin, dextrin, starch, gelatin, tragacanth, methylcellulose, sodium carboxymethylcellulose, a low melting wax, cocoa butter, and the like. A preferred form for oral use are capsules, which include the formulation of the active compound with encapsulating material as a carrier providing a capsule in which the active component with or without other carriers, is surrounded by a carrier, which is thus in association with it. Similarly, cachets and lozenges are included. Tablets, powders, capsules, pills, cachets, and lozenges can be used as solid dosage forms suitable for oral administration.

For preparing suppositories, a low melting wax, such as a mixture of fatty acid glycerides or cocoa butter, is first melted and the active component is dispersed homogeneously therein, as by stirring. The molten homogenous mixture is then poured into convenient size molds, allowed to cool, and thereby to solidify.

Liquid form preparations include solutions, suspensions, and emulsions such as water or water/propylene glycol solutions. For parenteral injection, liquid preparations can be formulated in solution in aqueous polyethylene glycol solution, isotonic saline, 5% aqueous glucose, and the like. Aqueous solutions suitable for oral use can be prepared by dissolving the active component in water and adding suitable colorants, flavors, stabilizing and thickening agents as desired. Aqueous suspensions suitable for oral use can be made by dispersing the finely divided active component in water and mixing with a viscous material, such as natural or synthetic gums, resins, methylcellulose, sodium carboxymethylcellulose, or other well-known suspending agents.

Also included are solid form preparations that are intended to be converted, shortly before use, to liquid form preparations for oral administration. Such liquid forms include solutions, suspensions, and emulsions. These preparations may contain, in addition to the active component, colorants, flavors, stabilizers, buffers, artificial and natural sweeteners, dispersants, thickeners, solubilizing agents, and the like. Waxes, polymers, microparticles, and the like can be utilized to prepare sustained-release dosage forms. Also, osmotic pumps can be employed to deliver the active compound uniformly over a prolonged period.

The pharmaceutical preparations for use in the invention are preferably in unit dosage form. In such form, the preparation is subdivided into unit doses containing appropriate quantities of the active component. The unit dosage form can be a packaged preparation, the package containing discrete quantities of preparation, such as packeted tablets, capsules, and powders in vials or ampules. Also, the unit dosage form can be a capsule, tablet, cachet, or lozenge itself, or it can be the appropriate number of any of these in packaged form.

The therapeutically effective dose of a compound of Formula I and/or Formula II will generally be from about 1 mg to about 100 mg/kg of body weight per day. Typical adult doses will be about 50 mg to about 800 mg per day. The

quantity of active component in a unit dose preparation may be varied or adjusted from about 0.1 mg to about 500 mg, preferably about 0.5 mg to 100 mg according to the particular application and the potency of the active component. The composition can, if desired, also contain other compatible therapeutic agents. A subject in need of treatment with a compound of Formula I and/or II is administered a dosage of about 1 to about 500 mg per day, either singly or in multiple doses over a 24-hour period.

The following compounds illustrate specific embodiments provided by the present invention, and the compounds listed below are among the preferred embodiments for use in treating neurodegenerative diseases:

8-(3-Phenoxy-benzyl)-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(2-Cyclopropyl-ethyl)-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(2-Naphthalen-2-yl-ethyl)-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(3,5-Dimethoxy-benzyl)-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Hex-2-ynyl-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(4-Methylsulfanyl-benzyl)-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(3,3-Dimethyl-butyl)-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(2-Phenethyl-benzyl)-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(2-Ethyl-hexyl)-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Cyclohex-3-enylmethyl-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Bicyclo[2.2.1]hept-2-ylmethyl-2-phenylamino-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-(4-Chloro-2-nitro-benzyl)-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(3-Ethyl-oxetan-3-ylmethyl)-2-phenylamino-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-[2-(2-Methoxy-ethoxy)-ethyl]-2-phenylamino-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-(2,2,3,3,3-Pentafluoro-propyl)-2-phenylamino-8H-pyrido[2,3-d]-pyrimidin-7-one;

2-Phenylamino-8-(tetrahydro-furan-2-ylmethyl)-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-(3-Methyl-but-2-enyl)-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-[2-(4-tert-Butyl-phenoxy)-ethyl]-2-phenylamino-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-(4-Ethyl-benzyl)-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(2-Phenoxy-ethyl)-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(2-Methyl-allyl)-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(3-Methyl-benzyl)-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(4-Methyl-benzyl)-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(2-Butoxy-ethyl)-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

2-Phenylamino-8-(2,2,2-trifluoro-ethyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-Phenylamino-8-(2-thiophen-2-yl-ethyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Benzo[1,3]dioxol-5-ylmethyl-2-phenylamino-8H-pyrido[2,3-]pyrimidin-7-one;

8-Cyclohexylmethyl-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(2-Ethoxy-ethyl)-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

2-Phenylamino-8-thiophen-2-ylmethyl-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Furan-2-ylmethyl-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(3-Phenyl-allyl)-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Furan-3-ylmethyl-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(3-Methoxy-propyl)-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(3-Methyl-bicyclo[2.2.1]hept-2-ylmethyl)-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

2-Phenylamino-8-(3-phenyl-prop-2-ynyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(2-Methyl-3-oxo-butyl)-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-[Bis-(4-fluoro-phenyl)-methyl]-2-phenylamino-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-[Cyclopropyl-(4-fluoro-phenyl)-methyl]-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(2-Isopropyl-cyclohexyl)-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(2,2,3,3,4,4,5,5,6,6,7,7-Dodecafluoro-1,1-dimethyl-heptyl)-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

2-Phenylamino-8-(1,7,7-trimethyl-bicyclo[2.2.1]hept-2-yl)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-Phenylamino-8-(2,2,2-trifluoro-1-phenyl-ethyl)-8H-pyrido[2,3-d]-pyrimidin-7-one;

2-Phenylamino-8-(2,2,2-trichloro-1-phenyl-ethyl)-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-(2,3-Dimethyl-cyclohexyl)-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

2-Phenylamino-8-(tetrahydro-pyran-4-yl)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Cyclohex-2-enyl-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

2-Phenylamino-8-(1,3,3-trimethyl-bicyclo[2.2.1]hept-2-yl)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Bicyclo[2.2.1]hept-5-en-2-yl-2-phenylamino-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-(1-Naphthalen-2-yl-ethyl)-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1-Methyl-2-phenyl-ethyl)-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(2,5-Dimethyl-cyclohexyl)-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(4-sec-Butyl-cyclohexyl)-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Cyclohex-3-enyl-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Indan-1-yl-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(2-Isopropyl-5-methyl-cyclohexyl)-2-phenylamino-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-(1-Naphthalen-2-yl-ethyl)-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(2,6-Dimethyl-cyclohexyl)-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(5-Isopropyl-2-methyl-cyclohexyl)-2-phenylamino-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-(1-Methyl-pent-2-ynyl)-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Bicyclo[2.2.1]hept-2-yl-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1-Methyl-2,2-diphenyl-ethyl)-2-phenylamino-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-[1-(4-Methoxy-phenyl)-ethyl]-2-phenylamino-8H-pyrido[2,3-d]-pyrimidin-7-one;

2-Phenylamino-8-(1,2,3,4-tetrahydro-naphthalen-2-yl)-8H-pyrido[2,3-d]-pyrimidin-7-one;

2-Phenylamino-8-(1-p-tolyl-ethyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Adamantan-2-yl-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1-Methyl-but-3-ynyl)-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Bicyclo[2.2.1]hept-2-yl-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1-Cyclohexyl-ethyl)-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Dicyclohexylmethyl-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

2-Phenylamino-8-(phenyl-o-tolyl-methyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-[1-(3,4-Dichloro-phenyl)-ethyl]-2-phenylamino-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-(1-Methyl-hexyl)-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Indan-2-yl-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-[1-(2-Bromo-phenyl)-ethyl]-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(2-Methoxy-1-methyl-ethyl)-2-phenylamino-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-(1-Methyl-2-phenyl-ethyl)-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1-Ethyl-propyl)-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(4-Isopropyl-cyclohexyl)-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Acenaphthen-1-yl-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(2-Oxo-cyclohexyl)-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

2-Phenylamino-8-(1,2,3,4-tetrahydro-naphthalen-1-yl)-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-(1-Methyl-heptyl)-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

2-Phenylamino-8-[phenyl-(2-trifluoromethyl-phenyl)-methyl]-8H-pyrido[2,3-d]pyrimidin-7-one;

2-Phenylamino-8-(1,7,7-trimethyl-bicyclo[2.2.1]hept-2-yl)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1,1-Dioxo-tetrahydro-1-δ^6-thiophen-3-yl)-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1-Biphenyl-4-yl-ethyl)-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(3-Methyl-cyclohexyl)-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Benzhydryl-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

2-Phenylamino-8-(9H-xanthen-9-yl)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1-Pentyl-prop-2-ynyl)-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(Octahydro-inden-5-yl)-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

2-Phenylamino-8-(2-phenyl-cyclohexyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(3,5-Dimethyl-cyclohexyl)-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(4-tert-Butyl-cyclohexyl)-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(2-Methyl-cyclohexyl)-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-[3-Phenoxy-1-(2-phenoxy-ethyl)-propyl]-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1-Cyclohexyl-propyl)-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1-Ethyl-prop-2-ynyl)-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

2-Phenylamino-8-(1-phenyl-heptyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-[(4-Methoxy-phenyl)-pyridin-2-yl-methyl]-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Bicyclohexyl-4-yl-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(4-Methyl-cyclohexyl)-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Cyclohexyl-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(Cyclohexyl-phenyl-methyl)-2-phenylamino-8H-pyrido[2,3-d]-pyrimidin-7-one;

2-Phenylamino-8-(1-phenyl-propyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-Phenylamino-8-(1-phenyl-prop-2-ynyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-Phenylamino-8-(2-phenyl-[1,3]dioxan-5-yl)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-Phenylamino-8-(2,2,2-trifluoro-1-trifluoromethyl-ethyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(7-Oxo-2-phenylamino-7H-pyrido[2,3-d]pyrimidin-8-yl)-propionitrile;

8-Cyclooctyl-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(Decahydro-naphthalen-2-yl)-2-phenylamino-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-(9H-Fluoren-9-yl)-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-[4-(1,1-Dimethyl-propyl)-cyclohexyl]-2-phenylamino-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-(10,11-Dihydro-5H-dibenzo[a,d]cyclohepten-5-yl)-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

2-Phenylamino-8-[2,2,2-trichloro-1-(4-fluoro-phenyl)-ethyl]-8H-pyrido[2,3-d]pyrimidin-7-one;

2-Phenylamino-8-(3,3,5-trimethyl-cyclohexyl)-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-(3-Phenoxy-benzyl)-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-]-pyrimidin-7-one;

8-(2-Cyclopropyl-ethyl)-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-]pyrimidin-7-one;

8-(2-Naphthalen-2-yl-ethyl)-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(3,5-Dimethoxy-benzyl)-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Hex-2-ynyl-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-(4-Methylsulfanyl-benzyl)-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(3,3-Dimethyl-butyl)-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(2-Phenethyl-benzyl)-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(2-Ethyl-hexyl)-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-Cyclohex-3-enylmethyl-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Bicyclo[2.2.1]hept-2-ylmethyl-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(4-Chloro-2-nitro-benzyl)-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(3-Ethyl-oxetan-3-ylmethyl)-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-[2-(2-Methoxy-ethoxy)-ethyl]-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(2,2,3,3,3-Pentafluoro-propyl)-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(4-Piperidin-1-yl-phenylamino)-8-(tetrahydro-furan-2-ylmethyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(3-Methyl-but-2-enyl)-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-]pyrimidin-7-one;

8-[2-(4-tert-Butyl-phenoxy)-ethyl]-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(4-Ethyl-benzyl)-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-(2-Phenoxy-ethyl)-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-(2-Methyl-allyl)-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-(3-Methyl-benzyl)-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-(4-Methyl-benzyl)-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-(2-Butoxy-ethyl)-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]-pyrimidin-7-one;

2-(4-Piperidin-1-yl-phenylamino)-8-(2,2,2-trifluoro-ethyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(4-Piperidin-1-yl-phenylamino)-8-(2-thiophen-2-yl-ethyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Benzo[1,3]dioxol-5-ylmethyl-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Cyclohexylmethyl-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-(2-Ethoxy-ethyl)-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]-pyrimidin-7-one;

2-(4-Piperidin-1-yl-phenylamino)-8-thiophen-2-ylmethyl-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Furan-2-ylmethyl-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-(3-Phenyl-allyl)-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-Furan-3-ylmethyl-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-(3-Methoxy-propyl)-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(3-Methyl-bicyclo[2.2.1]hept-2-ylmethyl)-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(3-Phenyl-prop-2-ynyl)-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(2-Methyl-3-oxo-butyl)-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-[Bis-(4-fluoro-phenyl)-methyl]-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-[Cyclopropyl-(4-fluoro-phenyl)-methyl]-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(2-Isopropyl-cyclohexyl)-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(2,2,3,3,4,4,5,5,6,6,7,7-Dodecafluoro-1,1-dimethyl-heptyl)-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(4-Piperidin-1-yl-phenylamino)-8-(1,7,7-trimethyl-bicyclo[2.2.1]hept-2-yl)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(4-Piperidin-1-yl-phenylamino)-8-(2,2,2-trifluoro-1-phenyl-ethyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(4-Piperidin-1-yl-phenylamino)-8-(2,2,2-trichloro-1-phenyl-ethyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(2,3-Dimethyl-cyclohexyl)-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(4-Piperidin-1-yl-phenylamino)-8-(tetrahydro-pyran-4-yl)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Cyclohex-2-enyl-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]-pyrimidin-7-one;

2-(4-Piperidin-1-yl-phenylamino)-8-(1,3,3-trimethyl-bicyclo[2.2.1]hept-2-yl)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Bicyclo[2.2.1]hept-5-en-2-yl-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1-Naphthalen-2-yl-ethyl)-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1-Methyl-2-phenyl-ethyl)-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(2,5-Dimethyl-cyclohexyl)-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(4-sec-Butyl-cyclohexyl)-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Cyclohex-3-enyl-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-Indan-1-yl-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-(2-Isopropyl-5-methyl-cyclohexyl)-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1-Naphthalen-2-yl-ethyl)-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(2,6-Dimethyl-cyclohexyl)-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(5-Isopropyl-2-methyl-cyclohexyl)-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1-Methyl-pent-2-ynyl)-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Bicyclo[2.2.1]hept-2-yl-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1-Methyl-2,2-diphenyl-ethyl)-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-[1-(4-Methoxy-phenyl)-ethyl]-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(4-Piperidin-1-yl-phenylamino)-8-(1,2,3,4-tetrahydro-naphthalen-2-yl)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(4-Piperidin-1-yl-phenylamino)-8-(1-p-tolyl-ethyl)-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-Adamantan-2-yl-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-(1-Methyl-but-3-ynyl)-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Bicyclo[2.2.1]hept-2-yl-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1-Cyclohexyl-ethyl)-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Dicyclohexylmethyl-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(Phenyl-o-tolyl-methyl)-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-[1-(3,4-Dichloro-phenyl)-ethyl]-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1-Methyl-hexyl)-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-Indan-2-yl-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-[1-(2-Bromo-phenyl)-ethyl]-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(2-Methoxy-1-methyl-ethyl)-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1-Methyl-2-phenyl-ethyl)-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1-Ethyl-propyl)-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-(4-Isopropyl-cyclohexyl)-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Acenaphthen-1-yl-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-(2-Oxo-cyclohexyl)-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(4-Piperidin-1-yl-phenylamino)-8-(1,2,3,4-tetrahydro-naphthalen-1-yl)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1-Methyl-heptyl)-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-[Phenyl-(2-trifluoromethyl-phenyl)-methyl]-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(4-Piperidin-1-yl-phenylamino)-8-(1,7,7-trimethyl-bicyclo[2.2.1]hept-2-yl)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1,1-Dioxo-tetrahydro-δ^6-thiophen-3-yl)-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1-Biphenyl-4-yl-ethyl)-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(3-Methyl-cyclohexyl)-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Benzhydryl-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]-pyrimidin-7-one;

2-(4-Piperidin-1-yl-phenylamino)-8-(9H-xanthen-9-yl)-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-(1-Pentyl-prop-2-ynyl)-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(Octahydro-inden-5-yl)-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(2-Phenyl-cyclohexyl)-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(3,5-Dimethyl-cyclohexyl)-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(4-tert-Butyl-cyclohexyl)-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(2-Methyl-cyclohexyl)-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-[3-Phenoxy-1-(2-phenoxy-ethyl)-propyl]-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1-Cyclohexyl-propyl)-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1-Ethyl-prop-2-ynyl)-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1-Phenyl-heptyl)-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-[(4-Methoxy-phenyl)-pyridin-2-yl-methyl]-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Bicyclohexyl-4-yl-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-(4-Methyl-cyclohexyl)-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Cyclohexyl-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-(Cyclohexyl-phenyl-methyl)-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1-Phenyl-propyl)-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-(1-Phenyl-prop-2-ynyl)-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(2-Phenyl-[1,3]dioxan-5-yl)-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(4-Piperidin-1-yl-phenylamino)-8-(2,2,2-trifluoro-1-trifluoromethyl-ethyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-[7-Oxo-2-(4-piperidin-1-yl-phenylamino)-7H-pyrido[2,3-d]pyrimidin-8-yl]-propionitrile;

8-Cyclooctyl-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-(Decahydro-naphthalen-2-yl)-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(9H-Fluoren-9-yl)-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-[4-(1,1-Dimethyl-propyl)-cyclohexyl]-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(10,11-Dihydro-5H-dibenzo[a,d]cyclohepten-5-yl)-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(4-Piperidin-1-yl-phenylamino)-8-[2,2,2-trichloro-1-(4-fluoro-phenyl)-ethyl]-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(4-Piperidin-1-yl-phenylamino)-8-(3,3,5-trimethyl-cyclohexyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-[4-(4-Methyl-piperazin-1-yl)-phenylamino]-8-(3-phenoxy-benzyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(2-Cyclopropyl-ethyl)-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

2-[4-(4-Methyl-piperazin-1-yl)-phenylamino]-8-(2-naphthalen-2-yl-ethyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(3,5-Dimethoxy-benzyl)-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Hex-2-ynyl-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

2-[4-(4-Methyl-piperazin-1-yl)-phenylamino]-8-(4-methylsulfanyl-benzyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-[4-(4-Methyl-piperazin-1-yl)-phenylamino]-8-(4-methylsulfanyl-benzyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(3,3-Dimethyl-butyl)-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

2-[4-(4-Methyl-piperazin-1-yl)-phenylamino]-8-(2-phenethyl-benzyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(2-Ethyl-hexyl)-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Cyclohex-3-enylmethyl-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Bicyclo[2.2.1]hept-2-ylmethyl-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(4-Chloro-2-nitro-benzyl)-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(3-Ethyl-oxetan-3-ylmethyl)-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

8-[2-(2-Methoxy-ethoxy)-ethyl]-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

2-[4-(4-Methyl-piperazin-1-yl)-phenylamino]-8-(2,2,3,3,3-pentafluoro-propyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-[4-(4-Methyl-piperazin-1-yl)-phenylamino]-8-(tetrahydro-furan-2-ylmethyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(3-Methyl-but-2-enyl)-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

8-[2-(4-tert-Butyl-phenoxy)-ethyl]-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(4-Ethyl-benzyl)-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

2-[4-(4-Methyl-piperazin-1-yl)-phenylamino]-8-(2-phenoxy-ethyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(2-Methyl-allyl)-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(3-Methyl-benzyl)-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(4-Methyl-benzyl)-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(2-Butoxy-ethyl)-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

2-[4-(4-Methyl-piperazin-1-yl)-phenylamino]-8-(2,2,2-trifluoro-ethyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-[4-(4-Methyl-piperazin-1-yl)-phenylamino]-8-(2-thiophen-2-yl-ethyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Benzo[1,3]dioxol-5-ylmethyl-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Cyclohexylmethyl-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(2-Ethoxy-ethyl)-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

2-[4-(4-Methyl-piperazin-1-yl)-phenylamino]-8-thiophen-2-ylmethyl-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Furan-2-ylmethyl-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

2-[4-(4-Methyl-piperazin-1-yl)-phenylamino]-8-(3-phenyl-allyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Furan-3-ylmethyl-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(3-Methoxy-propyl)-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(3-Methyl-bicyclo[2.2.1]hept-2-ylmethyl)-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

2-[4-(4-Methyl-piperazin-1-yl)-phenylamino]-8-(3-phenyl-prop-2-ynyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(2-Methyl-3-oxo-butyl)-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

8-[Bis-(4-fluoro-phenyl)-methyl]-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

8-[Cyclopropyl-(4-fluoro-phenyl)-methyl]-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(2-Isopropyl-cyclohexyl)-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(2,2,3,3,4,4,5,5,6,6,7,7-Dodecafluoro-1,1-dimethyl-heptyl)-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

2-[4-(4-Methyl-piperazin-1-yl)-phenylamino]-8-(1,7,7-trimethyl-bicyclo[2.2.1]hept-2-yl)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-[4-(4-Methyl-piperazin-1-yl)-phenylamino]-8-(2,2,2-trifluoro-1-phenyl-ethyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-[4-(4-Methyl-piperazin-1-yl)-phenylamino]-8-(2,2,2-trichloro-1-phenyl-ethyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(2,3-Dimethyl-cyclohexyl)-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

2-[4-(4-Methyl-piperazin-1-yl)-phenylamino]-8-(tetrahydro-pyran-4-yl)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Cyclohex-2-enyl-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

2-[4-(4-Methyl-piperazin-1-yl)-phenylamino]-8-(1,3,3-trimethyl-bicyclo[2.2.1]hept-2-yl)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Bicyclo[2.2.1]hept-5-en-2-yl-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

2-[4-(4-Methyl-piperazin-1-yl)-phenylamino]-8-(1-naphthalen-2-yl-ethyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1-Methyl-2-phenyl-ethyl)-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(2,5-Dimethyl-cyclohexyl)-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(4-sec-Butyl-cyclohexyl)-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Cyclohex-3-enyl-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Indan-1-yl-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(2-Isopropyl-5-methyl-cyclohexyl)-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

2-[4-(4-Methyl-piperazin-1-yl)-phenylamino]-8-(1-naphthalen-2-yl-ethyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(2,6-Dimethyl-cyclohexyl)-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(5-Isopropyl-2-methyl-cyclohexyl)-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1-Methyl-pent-2-ynyl)-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Bicyclo[2.2.1]hept-2-yl-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1-Methyl-2,2-diphenyl-ethyl)-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

8-[1-(4-Methoxy-phenyl)-ethyl]-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

2-[4-(4-Methyl-piperazin-1-yl)-phenylamino]-8-(1,2,3,4-tetrahydro-naphthalen-2-yl)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-[4-(4-Methyl-piperazin-1-yl)-phenylamino]-8-(1-p-tolyl-ethyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Adamantan-2-yl-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1-Methyl-but-3-ynyl)-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Bicyclo[2.2.1]hept-2-yl-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1-Cyclohexyl-ethyl)-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Dicyclohexylmethyl-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

2-[4-(4-Methyl-piperazin-1-yl)-phenylamino]-8-(phenyl-o-tolyl-methyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-[1-(3,4-Dichloro-phenyl)-ethyl]-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1-Methyl-hexyl)-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Indan-2-yl-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

8-[1-(2-Bromo-phenyl)-ethyl]-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(2-Methoxy-1-methyl-ethyl)-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1-Methyl-2-phenyl-ethyl)-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1-Ethyl-propyl)-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(4-Isopropyl-cyclohexyl)-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Acenaphthen-1-yl-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

2-[4-(4-Methyl-piperazin-1-yl)-phenylamino]-8-(2-oxo-cyclohexyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-[4-(4-Methyl-piperazin-1-yl)-phenylamino]-8-(1,2,3,4-tetrahydro-naphthalen-1-yl)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1-Methyl-heptyl)-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

2-[4-(4-Methyl-piperazin-1-yl)-phenylamino]-8-[phenyl-(2-trifluoromethyl-phenyl)-methyl]-8H-pyrido[2,3-d]pyrimidin-7-one;

2-[4-(4-Methyl-piperazin-1-yl)-phenylamino]-8-(1,7,7-trimethyl-bicyclo[2.2.1]hept-2-yl)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1,1-Dioxo-tetrahydro-δ^6-thiophen-3-yl)-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1-Biphenyl-4-yl-ethyl)-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(3-Methyl-cyclohexyl)-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Benzhydryl-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

2-[4-(4-Methyl-piperazin-1-yl)-phenylamino]-8-(9H-xanthen-9-yl)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-[4-(4-Methyl-piperazin-1-yl)-phenylamino]-8-(1-pentyl-prop-2-ynyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-[4-(4-Methyl-piperazin-1-yl)-phenylamino]-8-(octahydro-inden-5-yl)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-[4-(4-Methyl-piperazin-1-yl)-phenylamino]-8-(2-phenyl-cyclohexyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(3,5-Dimethyl-cyclohexyl)-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(4-tert-Butyl-cyclohexyl)-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(2-Methyl-cyclohexyl)-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

2-[4-(4-Methyl-piperazin-1-yl)-phenylamino]-8-[3-phenoxy-1-(2-phenoxy-ethyl)-propyl]-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1-Cyclohexyl-propyl)-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1-Ethyl-prop-2-ynyl)-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

2-[4-(4-Methyl-piperazin-1-yl)-phenylamino]-8-(1-phenyl-heptyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-[(4-Methoxy-phenyl)-pyridin-2-yl-methyl]-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Bicyclohexyl-4-yl-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(4-Methyl-cyclohexyl)-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Cyclohexyl-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(Cyclohexyl-phenyl-methyl)-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

2-[4-(4-Methyl-piperazin-1-yl)-phenylamino]-8-(1-phenyl-propyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-[4-(4-Methyl-piperazin-1-yl)-phenylamino]-8-(1-phenyl-prop-2-ynyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-[4-(4-Methyl-piperazin-1-yl)-phenylamino]-8-(2-phenyl-[1,3]dioxan-5-yl)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-[4-(4-Methyl-piperazin-1-yl)-phenylamino]-8-(2,2,2-trifluoro-1-trifluoromethyl-ethyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-{2-[4-(4-Methyl-piperazin-1-yl)-phenylamino]-7-oxo-7H-pyrido[2,3-d]pyrimidin-8-yl}-propionitrile;

8-Cyclooctyl-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(Decahydro-naphthalen-2-yl)-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(9H-Fluoren-9-yl)-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

8-[4-(1,1-Dimethyl-propyl)-cyclohexyl]-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(10,11-Dihydro-5H-dibenzo[a,d]cyclohepten-5-yl)-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

2-[4-(4-Methyl-piperazin-1-yl)-phenylamino]-8-[2,2,2-trichloro-1-(4-fluoro-phenyl)-ethyl]-8H-pyrido[2,3-d]pyrimidin-7-one;

2-[4-(4-Methyl-piperazin-1-yl)-phenylamino]-8-(3,3,5-trimethyl-cyclohexyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(3-Phenoxy-benzyl)-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-(2-Cyclopropyl-ethyl)-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(2-Naphthalen-2-yl-ethyl)-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(3,5-Dimethoxy-benzyl)-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Hex-2-ynyl-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-(4-Methylsulfanyl-benzyl)-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(3,3-Dimethyl-butyl)-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-(2-Phenethyl-benzyl)-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-(2-Ethyl-hexyl)-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-Cyclohex-3-enylmethyl-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Bicyclo[2.2.1]hept-2-ylmethyl-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(4-Chloro-2-nitro-benzyl)-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(3-Ethyl-oxetan-3-ylmethyl)-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-[2-(2-Methoxy-ethoxy)-ethyl]-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(2,2,3,3,3-Pentafluoro-propyl)-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(4-Pyrazol-1-yl-phenylamino)-8-(tetrahydro-furan-2-ylmethyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(3-Methyl-but-2-enyl)-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-[2-(4-tert-Butyl-phenoxy)-ethyl]-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(4-Ethyl-benzyl)-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-(2-Phenoxy-ethyl)-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-(2-Methyl-allyl)-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-(3-Methyl-benzyl)-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-(4-Methyl-benzyl)-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-(2-Butoxy-ethyl)-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]-pyrimidin-7-one;

2-(4-Pyrazol-1-yl-phenylamino)-8-(2,2,2-trifluoro-ethyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(4-Pyrazol-1-yl-phenylamino)-8-(2-thiophen-2-yl-ethyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Benzo[1,3]dioxol-5-ylmethyl-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Cyclohexylmethyl-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-(2-Ethoxy-ethyl)-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]-pyrimidin-7-one;

2-(4-Pyrazol-1-yl-phenylamino)-8-thiophen-2-ylmethyl-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-Furan-2-ylmethyl-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-(3-Phenyl-allyl)-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-Furan-3-ylmethyl-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-(3-Methoxy-propyl)-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-(3-Methyl-bicyclo[2.2.1]hept-2-ylmethyl)-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(3-Phenyl-prop-2-ynyl)-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(2-Methyl-3-oxo-butyl)-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-[Bis-(4-fluoro-phenyl)-methyl]-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-[Cyclopropyl-(4-fluoro-phenyl)-methyl]-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(2-Isopropyl-cyclohexyl)-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(2,2,3,3,4,4,5,5,6,6,7,7-Dodecafluoro-1,1-dimethyl-heptyl)-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(4-Pyrazol-1-yl-phenylamino)-8-(1,7,7-trimethyl-bicyclo[2.2.1]hept-2-yl)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(4-Pyrazol-1-yl-phenylamino)-8-(2,2,2-trifluoro-1-phenyl-ethyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(4-Pyrazol-1-yl-phenylamino)-8-(2,2,2-trichloro-1-phenyl-ethyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(2,3-Dimethyl-cyclohexyl)-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(4-Pyrazol-1-yl-phenylamino)-8-(tetrahydro-pyran-4-yl)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Cyclohex-2-enyl-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]-pyrimidin-7-one;

2-(4-Pyrazol-1-yl-phenylamino)-8-(1,3,3-trimethyl-bicyclo[2.2.1]hept-2-yl)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Bicyclo[2.2.1]hept-5-en-2-yl-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1-Naphthalen-2-yl-ethyl)-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1-Methyl-2-phenyl-ethyl)-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(2,5-Dimethyl-cyclohexyl)-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(4-sec-Butyl-cyclohexyl)-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Cyclohex-3-enyl-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-Indan-1-yl-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(2-Isopropyl-5-methyl-cyclohexyl)-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1-Naphthalen-2-yl-ethyl)-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(2,6-Dimethyl-cyclohexyl)-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(5-Isopropyl-2-methyl-cyclohexyl)-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1-Methyl-pent-2-ynyl)-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Bicyclo[2.2.1]hept-2-yl-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1-Methyl-2,2-diphenyl-ethyl)-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-[1-(4-Methoxy-phenyl)-ethyl]-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(4-Pyrazol-1-yl-phenylamino)-8-(1,2,3,4-tetrahydro-naphthalen-2-yl)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(4-Pyrazol-1-yl-phenylamino)-8-(1-p-tolyl-ethyl)-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-Adamantan-2-yl-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-(1-Methyl-but-3-ynyl)-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Bicyclo[2.2.1]hept-2-yl-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1-Cyclohexyl-ethyl)-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Dicyclohexylmethyl-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(Phenyl-o-tolyl-methyl)-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-[1-(3,4-Dichloro-phenyl)-ethyl]-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1-Methyl-hexyl)-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-Indan-2-yl-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-[1-(2-Bromo-phenyl)-ethyl]-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(2-Methoxy-1-methyl-ethyl)-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1-Methyl-2-phenyl-ethyl)-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1-Ethyl-propyl)-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-(4-Isopropyl-cyclohexyl)-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Acenaphthen-1-yl-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-(2-Oxo-cyclohexyl)-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]-pyrimidin-7-one;

2-(4-Pyrazol-1-yl-phenylamino)-8-(1,2,3,4-tetrahydro-naphthalen-1-yl)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1-Methyl-heptyl)-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-[Phenyl-(2-trifluoromethyl-phenyl)-methyl]-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(4-Pyrazol-1-yl-phenylamino)-8-(1,7,7-trimethyl-bicyclo[2.2.1]hept-2-yl)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1,1-Dioxo-tetrahydro-δ^6-thiophen-3-yl)-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1-Biphenyl-4-yl-ethyl)-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(3-Methyl-cyclohexyl)-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Benzhydryl-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]-pyrimidin-7-one;

2-(4-Pyrazol-1-yl-phenylamino)-8-(9H-xanthen-9-yl)-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-(1-Pentyl-prop-2-ynyl)-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(Octahydro-inden-5-yl)-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(2-Phenyl-cyclohexyl)-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(3,5-Dimethyl-cyclohexyl)-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(4-tert-Butyl-cyclohexyl)-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(2-Methyl-cyclohexyl)-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-[3-Phenoxy-1-(2-phenoxy-ethyl)-propyl]-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1-Cyclohexyl-propyl)-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1-Ethyl-prop-2-ynyl)-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1-Phenyl-heptyl)-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-[(4-Methoxy-phenyl)-pyridin-2-yl-methyl]-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Bicyclohexyl-4-yl-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-(4-Methyl-cyclohexyl)-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Cyclohexyl-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-(Cyclohexyl-phenyl-methyl)-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1-Phenyl-propyl)-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1-Phenyl-prop-2-ynyl)-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(2-Phenyl-[1,3]dioxan-5-yl)-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(4-Pyrazol-1-yl-phenylamino)-8-(2,2,2-trifluoro-1-trifluoromethyl-ethyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-[7-Oxo-2-(4-pyrazol-1-yl-phenylamino)-7H-pyrido[2,3-d]pyrimidin-8-yl]-propionitrile;

8-Cyclooctyl-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(Decahydro-naphthalen-2-yl)-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(9H-Fluoren-9-yl)-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-[4-(1,1-Dimethyl-propyl)-cyclohexyl]-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(10,11-Dihydro-5H-dibenzo[a,d]cyclohepten-5-yl)-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(4-Pyrazol-1-yl-phenylamino)-8-[2,2,2-trichloro-1-(4-fluoro-phenyl)-ethyl]-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(4-Pyrazol-1-yl-phenylamino)-8-(3,3,5-trimethyl-cyclohexyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Cyclopentyl-2-[4-(3-diethylamino-2-hydroxy-propoxy)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Cyclopentyl-2-[4-(2-hydroxy-3-morpholin-4-yl-propoxy)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Cyclohexyl-2-[4-(3-diethylamino-2-hydroxy-propoxy)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Cyclohexyl-2-[4-(2-hydroxy-3-morpholin-4-yl-propoxy)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Bicyclo[2.2.1]hept-2-yl-2-[4-(3-diethylamino-2-hydroxy-propoxy)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one; and

8-Bicyclo[2.2.1]hept-2-yl-2-[4-(2-hydroxy-3-morpholin-4-yl-propoxy)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one.

Compounds of Formulas I and II may be prepared according to the syntheses outlined in Schemes 1 through 9, *infra*. Although these schemes often indicate exact structures, those with ordinary skill in the art will appreciate that the methods apply widely to analogous compounds of Formula I and/or II, given appropriate consideration to protection and deprotection or reactive functional groups by methods standard to the art of organic chemistry. For example, hydroxy groups, in order to prevent unwanted side reactions, generally need to be converted to ethers or esters during chemical reactions at other sites in the molecule. The hydroxy protecting group is readily removed to provide the free hydroxy group. Amino groups and carboxylic acid groups are similarly derivatized to protect them against unwanted side reactions. Typical protecting groups and methods for attaching and cleaving them are described fully by Greene and Wuts in *Protective Groups in Organic Synthesis*, John Wiley and Sons, New

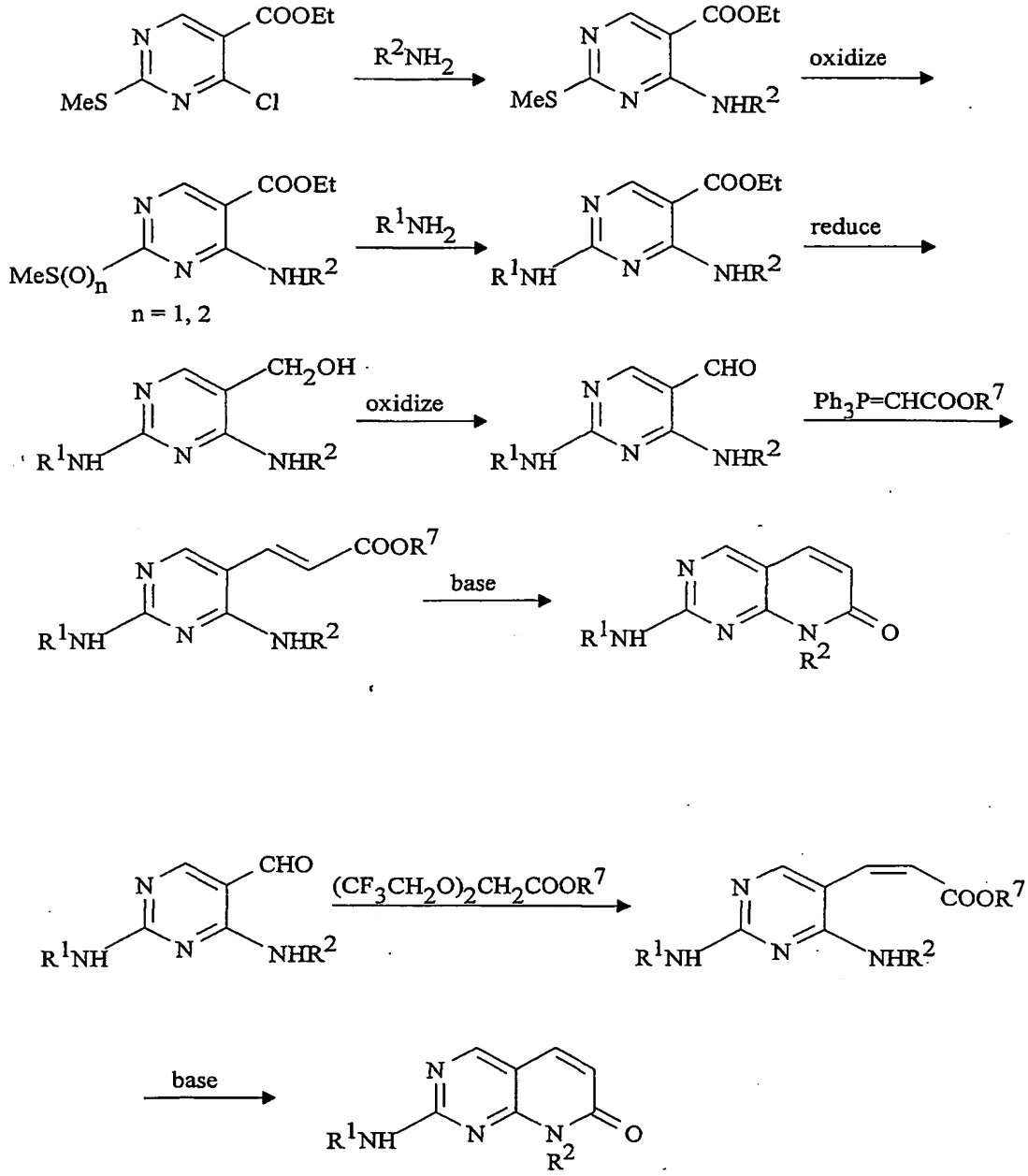
York, (2nd Ed., 1991), and McOmie, *Protective Groups in Organic Chemistry*, Plenum Press, New York, 1973.

Scheme 1 describes a typical method for the preparation of the pyrido[2,3-d]pyrimidin-7(8H)-ones of the invention. The synthesis begins with commercially available (Aldrich) 4-chloro-2-methylthio-pyrimidine-5-carboxylic acid ethyl ester. Displacement of the 4-chloro group with an amine in a solvent such as tetrahydrofuran in the presence or absence of a tertiary amine such as triethylamine provides the corresponding 4-amino-2-methylthio-pyrimidine-5-carboxylic acid ethyl ester. The amine used can be anhydrous or in an aqueous solution as with methyl or ethyl amine. The use of aqueous ammonium hydroxide provides the corresponding primary amine at position 4. Oxidation of the methylthio group with an oxidant such as an oxaziridine in a solvent such as chloroform at room temperature provides the methyl sulfoxide derivative. Displacement of the sulfoxide with an amine results in formation of the corresponding 2,4-diamino-pyrimidine-5-carboxylic acid ethyl ester. The temperature required for the displacement depends upon the amine used. Aromatic secondary and tertiary amines usually require higher temperatures than primary aliphatic or benzyl amines. When aromatic amines such as aniline are used, the reaction is usually run with the amine as the solvent at high temperatures. The ester group is sequentially reduced to the alcohol, preferably with lithium aluminum hydride in tetrahydrofuran, and then oxidized to the aldehyde. While sodium dichromate can be used as the oxidant, superior results are obtained with manganese II oxide in chloroform.

The 2,4-di-amino-pyrimidine-5-carboxaldehydes can be reacted with either a stabilized phosphorane, a phosphonate ester in the presence of a base, or any alternative Wittig or Horner-Emmons reagent to provide the corresponding unsaturated ester. The resulting double bond can be trans, cis, or a mixture of both. For example, reaction of a 2,4-diamino-pyrimidine-5-carboxaldehyde with an excess amount of the stabilized phosphorane (carbethoxymethylene)triphenylphosphorane in tetrahydrofuran at reflux temperature gives mainly, or in some cases exclusively, the trans unsaturated ethyl ester. Upon treatment with base, ring closure occurs to give the desired pyrido[2,3-d]pyrimidin-7(8H)-one. This reaction can be carried out using a

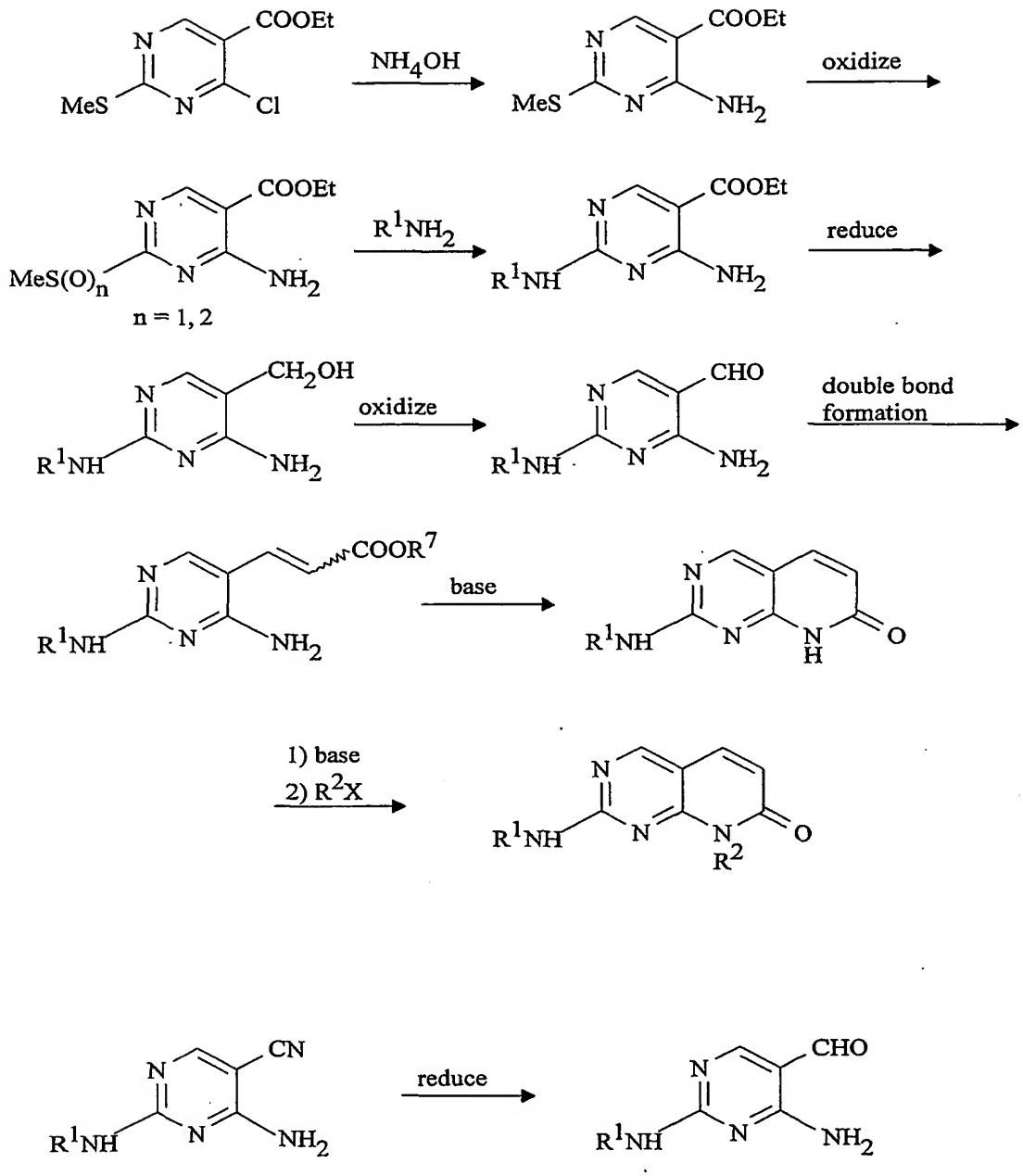
tertiary amine such as triethylamine or, preferably, N,N-diisopropylethyl amine as the solvent, with 1 to 10 equivalents of 1,8-diazabicyclo[5.4.0]undec-7-ene present. The reaction is carried out at elevated temperature, and is usually complete in 2 to 24 hours. Alternatively, the 2,4-diamino-pyrimidine-5-carboxaldehyde can be reacted with a phosphonate ester such as bis(2,2,2-trifluoroethyl)(methoxycarbonyl-methyl)-phosphonate using a strongly dissociated base (*Tetrahedron Lett.*, 1983:4405) to give predominately, if not exclusively, the cis unsaturated ester. Upon treatment with base under the conditions discussed previously, ring closure occurs.

SCHEME 1


COOEt
N
MeS
N
Cl
R^2NH_2
NHR2
oxidize
$MeS(O)_n$
n = 1, 2
R^1NH_2
R^1NH
reduce
CH_2OH
CHO
$Ph_3P=CHCOOR^7$
$COOR^7$
base
O
R^2
$(CF_3CH_2O)_2CH_2COOR^7$

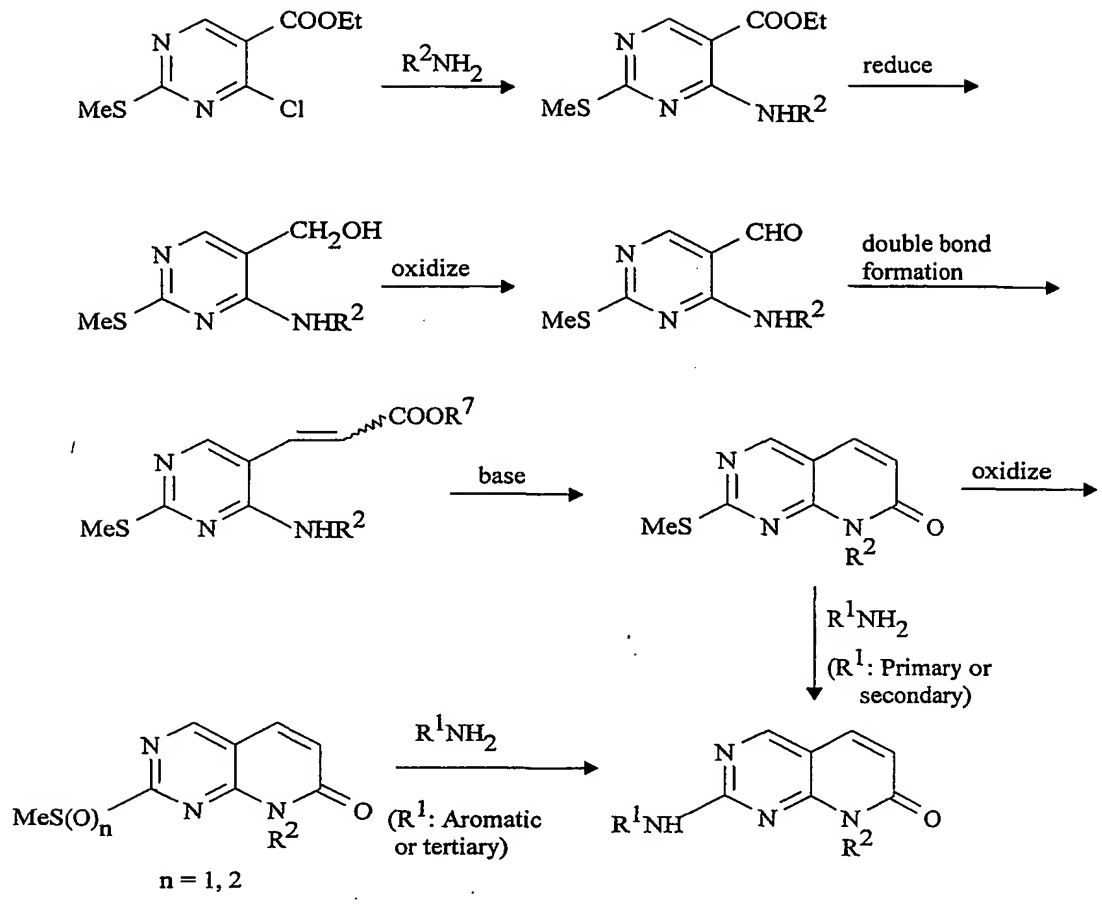
Scheme 2 depicts the preparation of pyrido[2,3-d]pyrimidin-7(8H)-ones of the invention where R^2 is H. The sequence of reactions is the same as Scheme 1, where the initial step uses ammonium hydroxide giving the 4-primary amino pyrimidine. The resultant pyrido[2,3-d]pyrimidin-7(8H)-ones where R^2 is equal to H can be alkylated at the 8-position by treatment with a base such as sodium hydride in a solvent such as dimethylformamide or tetrahydrofuran at temperatures ranging from 40°C to reflux, thus providing the corresponding pyrido[2,3-d]pyrimidin-7(8H)-ones where R^2 is other than H. The advantage of the route shown in Scheme 2 is that it allows for several R^2 analogs to be prepared from a common intermediate. The required aldehyde can also be obtained by reduction of the corresponding nitrile (*J. Org. Chem.*, 1960;82:5711) with a reducing agent, preferably diisobutylaluminum hydride.

SCHEME 2


COOEt
MeS
N
Cl
NH4OH
NH2
oxidize
MeS(O)n
n = 1, 2
R1NH2
R1NH
reduce
CH2OH
CHO
double bond formation
COOR7
base
O
H
1) base
2) R2X
R2
CN

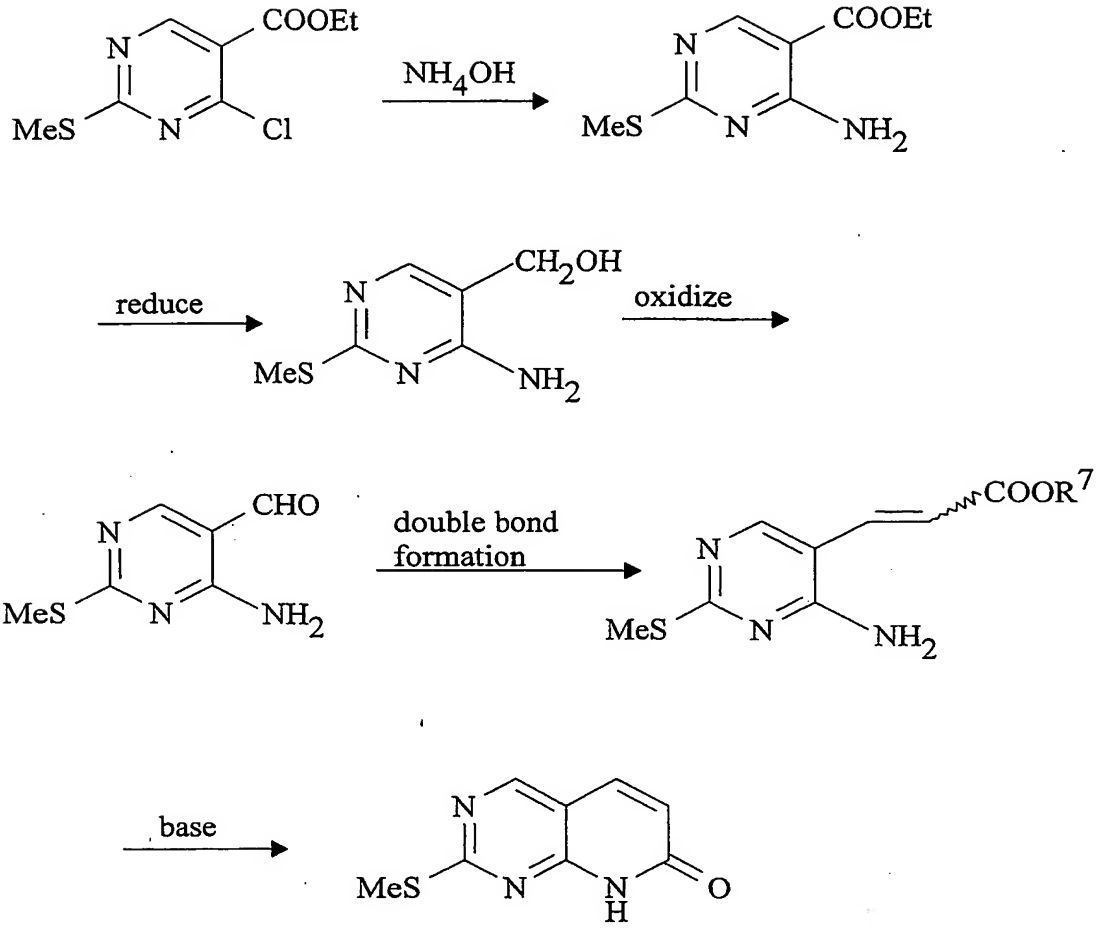
A route that allows for the preparation of several analogs with various R^1 groups from a common intermediate is shown in Scheme 3. The initial step is the same as in Scheme 1, but instead of oxidizing the methyl thio group, the ester is sequentially reduced and then oxidized using the conditions described in Scheme 1 to provide the corresponding 2-methylthio-4-amino-pyrimidine-5-carboxaldehyde. This aldehyde is converted to the corresponding unsaturated ester using the conditions described in Scheme 1. The methylthio group can be displaced directly with primary alkyl amines to give the pyrido[2,3-d]pyrimidin-7-(8H)-ones of the invention where R^1 is H or a primary alkyl group. The methylthio group can also be converted to the corresponding sulfoxide by treatment with an oxidizing agent, preferably an oxaziridine, in a solvent such as chloroform at room temperature. Alternatively, an oxidizing agent, such as m-chloroperbenzoic acid, can be used in excess to convert the methylthio derivative to the corresponding methyl sulfone. Upon treatment of these oxidized derivatives with an amine, usually with several equivalents of the amine at elevated temperatures in the case of aromatic or tertiary amines, pyrido[2,3-d]pyrimidin-7(8H)-ones of the invention with various R^1 groups are obtained. In some cases a solvent such as tetrahydrofuran or dimethylsulfoxide can be used.

SCHEME 3

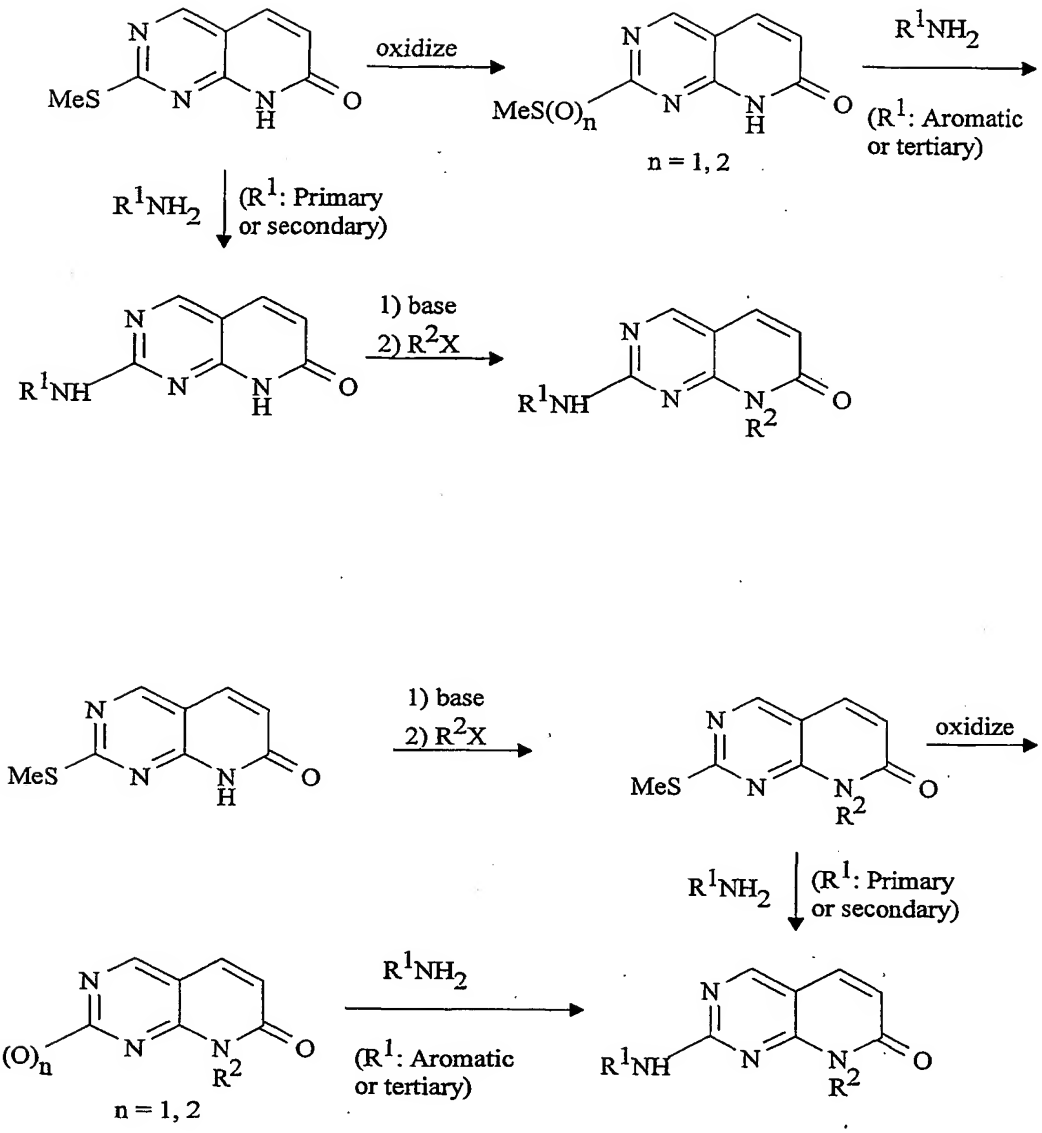

COOEt
N
MeS
N
Cl
R^2NH_2
COOEt
N
MeS
N
NHR^2
reduce
CH_2OH
N
MeS
N
NHR^2
oxidize
CHO
N
MeS
N
NHR^2
double bond formation
$COOR^7$
N
MeS
N
NHR^2
base
N
MeS
N
N
O
R^2
oxidize
R^1NH_2
(R^1: Primary or secondary)
N
$MeS(O)_n$
N
N
O
R^2
n = 1, 2
R^1NH_2
(R^1: Aromatic or tertiary)
N
R^1NH
N
N
O
R^2

The most convergent route to the compounds of the invention where X is O is via the synthesis of 2-methanesulfanyl-8H-pyrido[2,3-d]pyrimidin-7-one which is depicted in Scheme 4. This key intermediate is prepared by the methods discussed in the previous schemes and is converted to the compounds of the invention by 2 routes, shown in Scheme 5. In the first, the methylthio group is converted to an amino group, in some cases via an oxidized intermediate. These derivatives are then alkylated at N8 to give the desired compounds. Alternatively, 2-methanesulfanyl-8H-pyrido[2,3-d]pyrimidin-7-one is first alkylated at N8, then the methylthio group, or an oxidized derivative, is displaced by an amine.

SCHEME 4

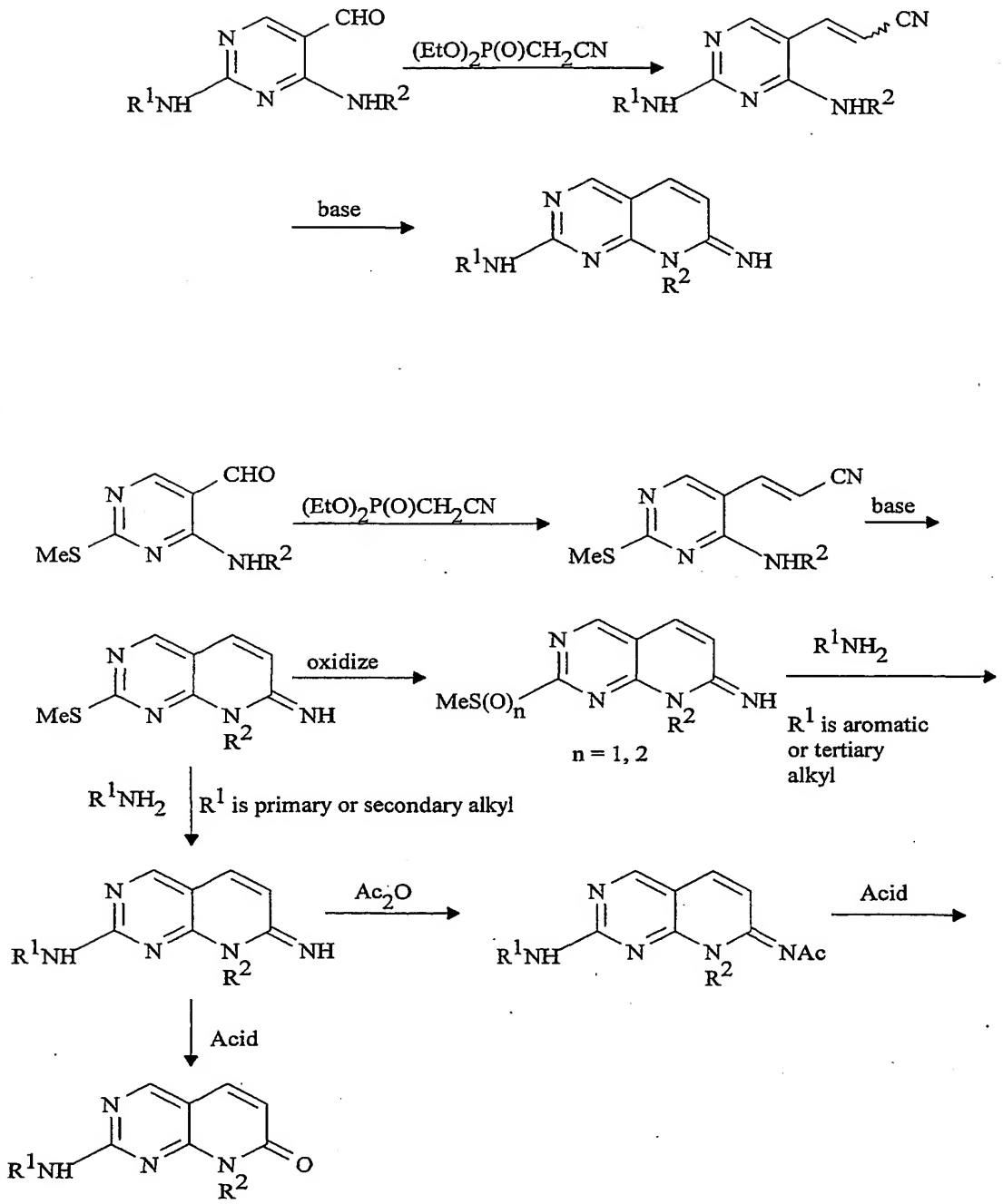

COOEt
N
MeS
N
Cl
NH4OH
COOEt
N
MeS
N
NH2
reduce
CH2OH
N
MeS
N
NH2
oxidize
CHO
N
MeS
N
NH2
double bond
formation
COOR7
N
MeS
N
NH2
base
N
MeS
N
N
H
O

SCHEME 5



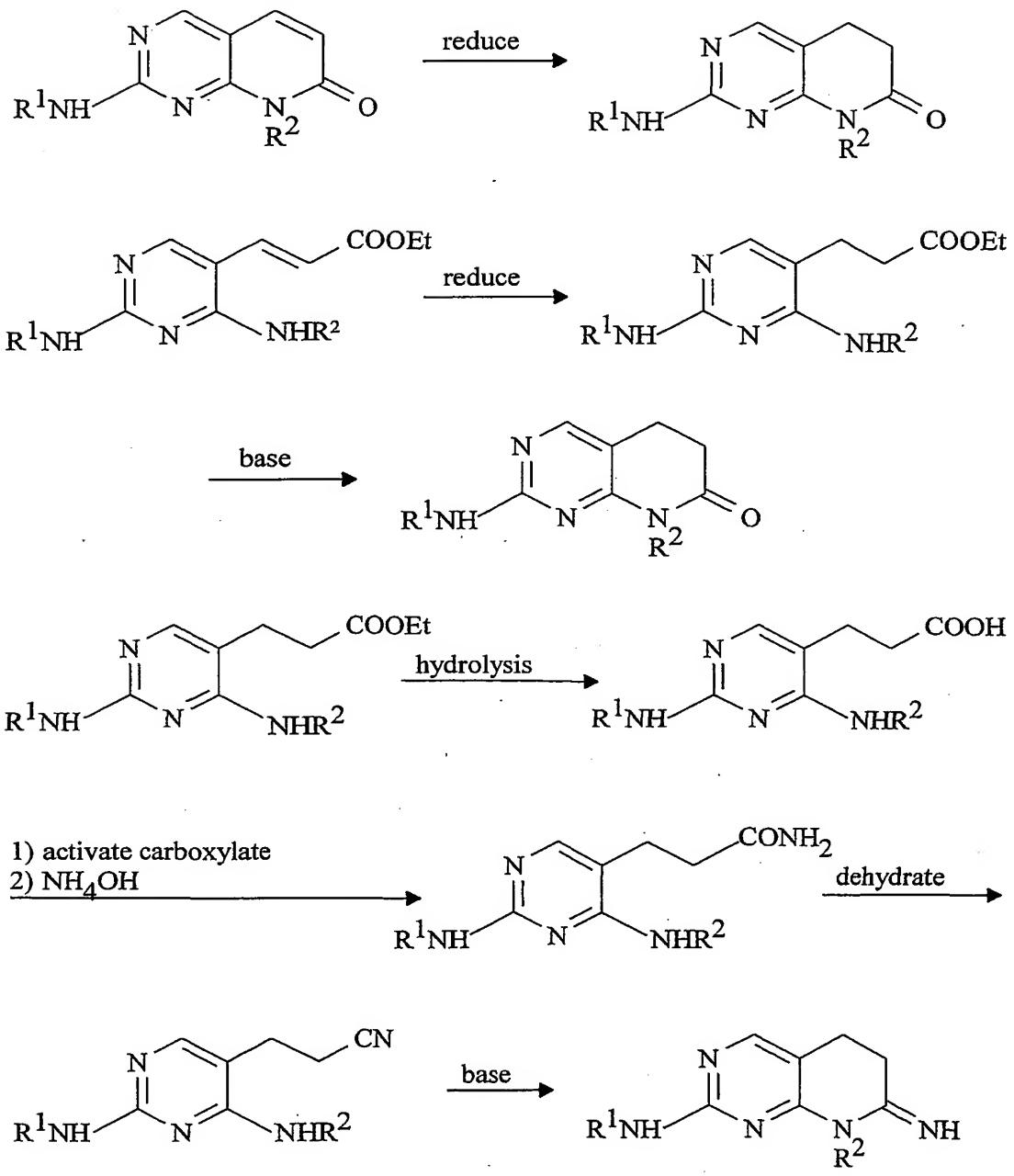
Scheme 6 describes a typical method for the preparation of the pyrido[2,3-d]pyrimidin-7(8H)-imines of the invention (X = NH). The synthesis begins with the 2,4-diamino-pyrimidine-5-carboxaldehyde previously described in Scheme 1. Reaction with diethyl cyanomethylphosphonate in the presence of a base, such as sodium hydride, in a solvent such as tetrahydrofuran, provides the corresponding unsaturated nitrile. This nitrile is then cyclized to give the pyrido[2,3-d]pyrimidin-7(8H)-imine under the same conditions used to prepare the pyrido[2,3-d]pyrimidin-7(8H)-ones of Scheme 1. Alternatively, the pyrimidine-5-carboxaldehyde can contain a methylthio group at C_2. After formation of the unsaturated nitrile followed by ring closure, the methylthio group at C_2 can be converted to an amino group by the methology previously mentioned. The pyrido[2,3-d]pyrimidin-7(8H)-imines can also be converted to the pyrido[2,3-d]pyrimidin-7(8H)-ones by direct hydrolysis with concentrated acid, such as hydrochloric acid, at elevated temperatures. A milder method can also be used where the imine is first acylated with acetic anhydride. The hydrolysis of this acyl intermediate to the 7-one occurs under shorter reaction time and lower reaction temperatures.

SCHEME 6


CHO
$(EtO)_2P(O)CH_2CN$
CN
R^1NH
NHR^2
base
NH
MeS
oxidize
$MeS(O)_n$
n = 1, 2
R^1NH_2
R^1 is aromatic or tertiary alkyl
R^1 is primary or secondary alkyl
Ac_2O
NAc
Acid
O

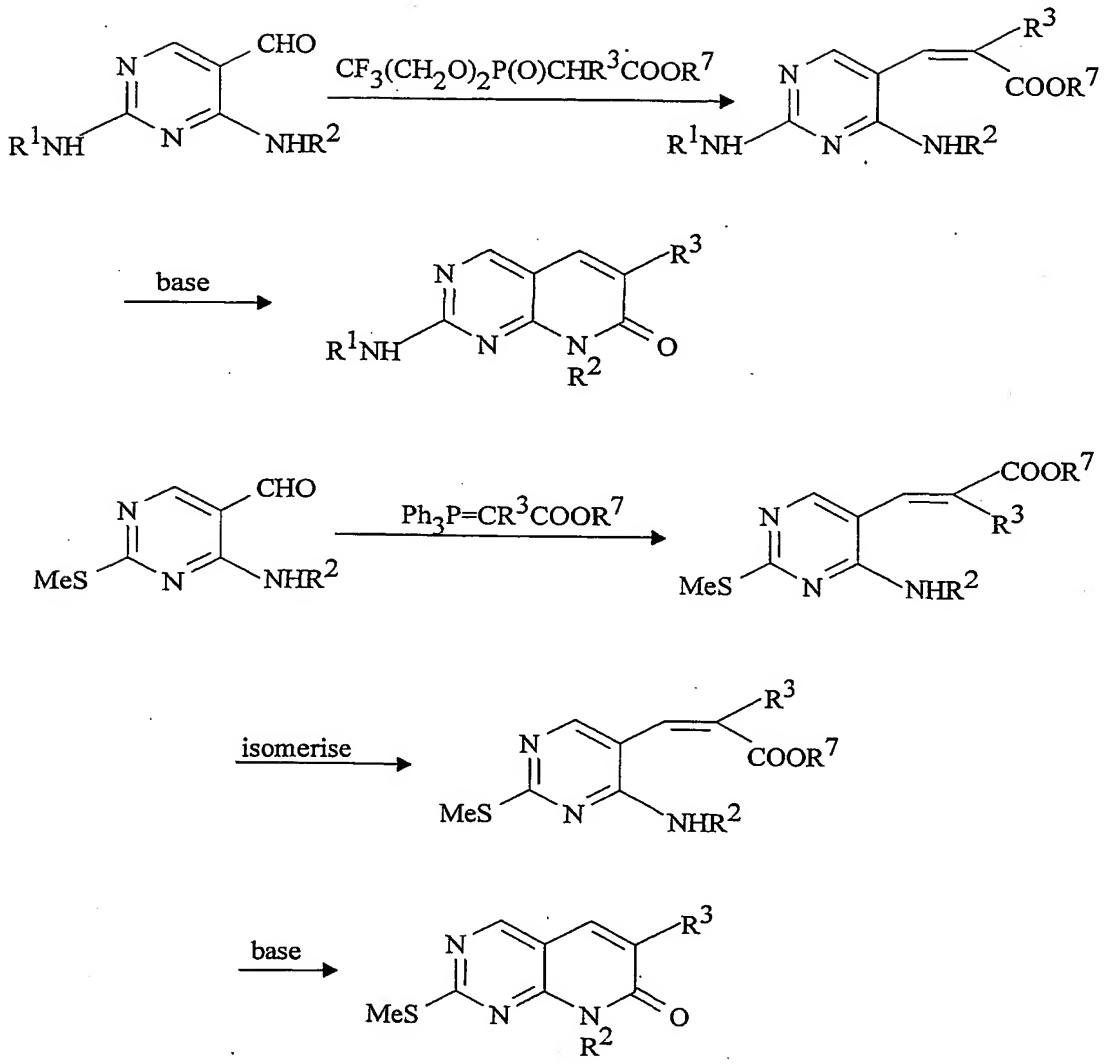
As shown in Scheme 7, those compounds where there is no double bond between C_5 and C_6 can be prepared by direct reduction of the double bond for those cases where X is O. Alternatively, a more preferred route is to reduce the double bond of the precursor unsaturated ester. This can be accomplished with a metal catalyst, such as palladium, in the presence of hydrogen under pressure. This saturated ester is then cyclized using the conditions discussed previously. Due to the propensity of the imine or nitrile group to be reduced under the conditions used to reduce the carbon-carbon double bond, a different route is required to prepare the compounds of the invention without a double bond at C_5-C_6 for those cases where X is NH. The saturated ester is hydrolyzed to the acid and then converted to the primary amide, by activation of the carboxylate with an acid chloride or N,N-carbonyldiimidazole, followed by treatment with ammonia gas or aqueous ammonium hydroxide. The primary amide is dehydrated to the corresponding nitrile with a reagent such as phosphorous pentoxide. This saturated nitrile is then cyclized using the conditions described previously.

SCHEME 7



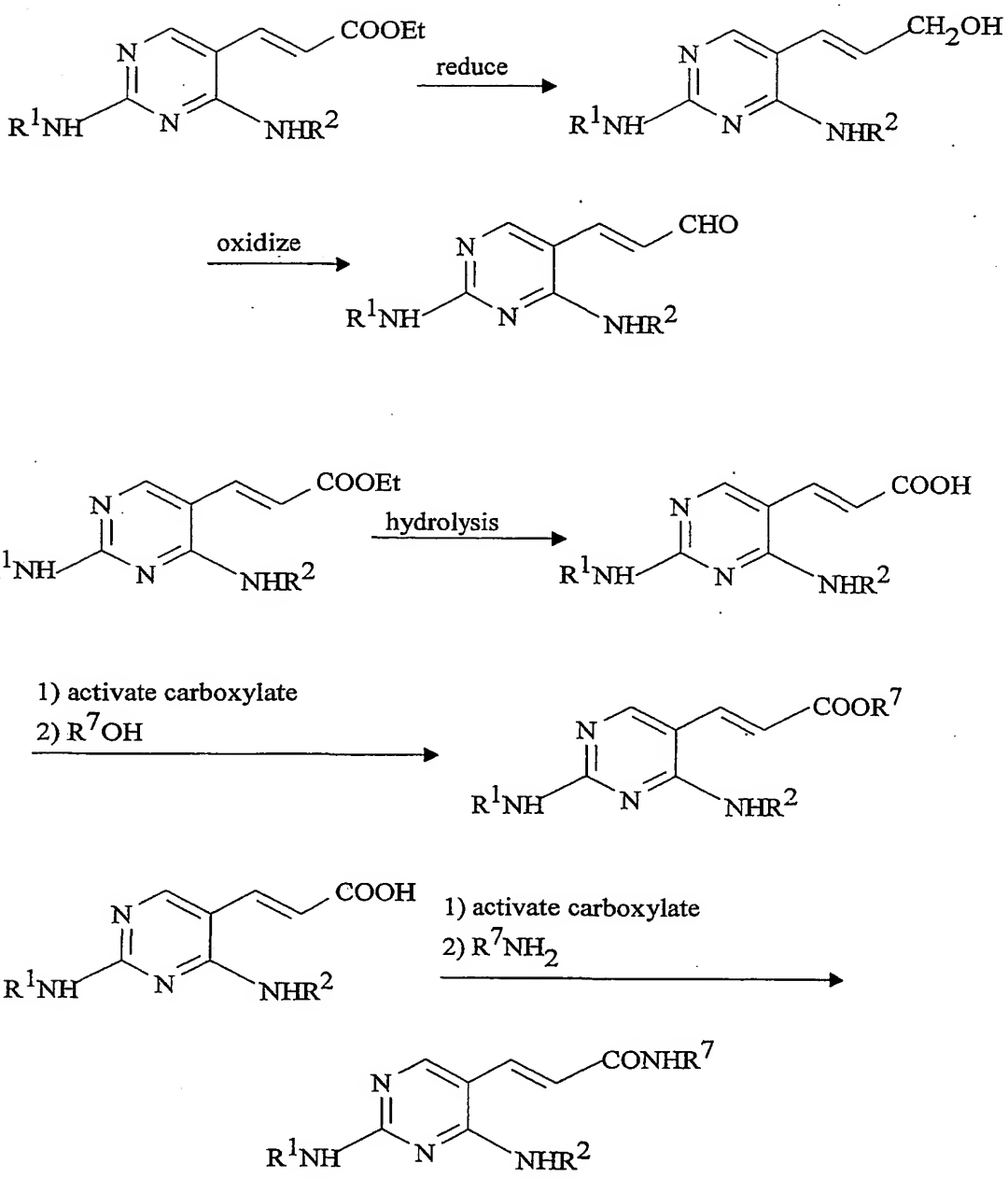
It should be noted that while the routes depicted in the earlier schemes showed the preparation of the pyrido[2,3-d]pyrimidin-7(8H)-ones of the invention where R^3 is H, these routes can be readily modified to prepare compounds where R^3 is lower alkyl, as shown in Scheme 8. Treatment with base provides compounds of the invention where X is O and R^3 is lower alkyl. Alternatively, these same reactions can be carried out on the 2-methylthio-4-amino-pyrimidine-5-carboxaldehyde and, after cyclization, the 2-methylthio group can be converted to the corresponding amine. Suitable modification of Scheme 6 would lead to the preparation of the pyrido[2,3-d]pyrimidin-7(8H)-imines of the invention where R^3 is lower alkyl.

SCHEME 8



Additional 2,4-diaminopyrimidines of the invention can be prepared as shown in Scheme 9. For example, those analogs where Z is CH_2OH are prepared by reduction of the ester with a reducing agent such as an excess of diisobutylaluminum hydride in a solvent such as tetrahydrofuran or chloroform. Subsequent oxidation with an oxidizing agent such as manganese oxide, or Swern's conditions, provides the compound where Z is CHO. Compounds where Z is $COOR^7$ or $CONHR^7$ can be obtained from the compound where Z is COOH. Activation of the carboxylate with an acid chloride or 1,1-carbonyldiimidazole, followed by addition of an alcohol of formula R^7OH or an amine of formula R^7NH_2, would provide those compounds where Z is $COOR^7$ and $CONHR^7$, respectively.

SCHEME 9



An alternative method for preparing the compounds of Formulas I and II comprises reacting a 2-halo pyridopyrimidine, for instance, with a group such as R^1NH, for instance an aryl amine or heteraryl amine. The reactants typically are mixed together in a mutual solvent such as dioxane and stirred for several hours at an elevated temperature of about 100°C. This process can be used to prepare numerous compounds by combinatorial synthetic array methodologies.

EXAMPLES

The following examples are for illustrative purposes only and are not intended, nor should they be construed as limiting the invention in any manner. Those skilled in the art will appreciate that variations and modifications can be made without violating the spirit or scope of the invention.

EXAMPLE 1

4-Ethylamino-2-methanesulfanyl-pyrimidine-5-carboxylic acid ethyl ester

To a room temperature solution of 4-chloro-2-methanesulfanyl-pyrimidine-5-carboxylic acid ethyl ester (10.00 g , 43.10 mmol) in 150 mL of tetrahydrofuran was added triethylamine (18.5 mL, 133 mmol) followed by 9 mL of a 70% aqueous solution of ethylamine. The solution was stirred for 30 minutes then concentrated in vacuo and partitioned between chloroform and saturated aqueous sodium bicarbonate. The organic layer was dried over magnesium sulfate, filtered, and concentrated to provide 9.32 g (90%) of 4-ethylamino-2-methanesulfanyl-pyrimidine-5-carboxylic acid ethyl ester as an oil.

Analysis calculated for $C_{10}H_{15}N_3O_2S$: C, 49.77; H, 6.27; N, 17.41.

Found: C, 49.77; H, 6.24; N, 17.30.

EXAMPLE 2

(4-Ethylamino-2-methanesulfanyl-pyrimidin-5-yl)-methanol

A solution of 4-ethylamino-2-methanesulfanyl-pyrimidine-5-carboxylic acid ethyl ester (8.93 g, 37.1 mmol) in 100 mL of tetrahydrofuran was added dropwise to a room temperature suspension of lithium aluminum hydride (2.30 g, 60.5 mmol) in 100 mL of tetrahydrofuran. After 10 minutes, the reaction was carefully quenched with 4.5 mL of water, 4.5 mL of 15% NaOH, and an

additional 16 mL of water, and the mixture was stirred for 1.5 hours. The white precipitate was removed by filtration, washing with ethyl acetate. The filtrate was concentrated in vacuo and 1:1 hexane:ethyl acetate was added. The solids were collected to give 6.77 g (92%) of (4-ethylamino-2-methanesulfanyl-pyrimidin-5-yl)-methanol, mp 152-156°C.

Analysis calculated for $C_8H_{13}N_3OS$: C, 48.22; H, 6.58; N, 21.09.

Found: C, 48.14; H, 6.61; N, 20.85.

EXAMPLE 3

4-Ethylamino-2-methanesulfanyl-pyrimidine-5-carboxaldehyde

To (4-ethylamino-2-methanesulfanyl-pyrimidin-5-yl)-methanol (6.44 g, 32.4 mmol) in 600 mL of chloroform was added manganese oxide (21.0 g, 241 mmol). The suspension was stirred at room temperature for 2 hours and an additional 5.5 g of manganese oxide was added. Stirring was continued for 4.5 hours. The mixture was filtered through celite, washing with chloroform. The filtrate was concentrated in vacuo to give 6.25 g (97%) of 4-ethylamino-2-methanesulfanyl-pyrimidine-5-carboxaldehyde, mp 58-61°C.

Analysis calculated for $C_8H_{11}N_3OS$: C, 48.71; H, 5.62; N, 21.30.

Found: C, 48.62; H, 5.60; N, 21.28.

EXAMPLE 4

4-Ethylamino-2-methanesulfinyl-pyrimidine-5-carboxylic acid ethyl ester

To a room temperature solution of 4-ethylamino-2-methanesulfanyl-5-pyrimidinecarboxylate ethyl ester (2.011 g , 8.34 mmol) in 70 mL of chloroform was added (±)-*trans*-2-(phenylsulfonyl)-3-phenyloxaziridine (2.70 g, 10.34 mmol). The solution was stirred at room temperature for 7 hours then concentrated in vacuo. The residue was purified by flash chromatography, eluting with a gradient of ethyl acetate to 3% methanol in ethyl acetate, to provide 2.07 g (97%) of 4-ethylamino-2-methanesulfinyl-pyrimidine-5-carboxylic acid ethyl ester, mp 54-56°C.

Analysis calculated for $C_{10}H_{15}N_3O_3S$: C, 46.68; H, 5.88; N, 16.33.

Found: C, 46.56; H, 5.68; N, 16.23.

EXAMPLE 5

4-Ethylamino-2-phenylamino-pyrimidine-5-carboxylic acid ethyl ester

A solution of 4-ethylamino-2-methanesulfinyl-pyrimidine-5-carboxylic acid ethyl ester (5.38 g, 20.9 mmol) in 4 mL of aniline was heated at 130°C for 1 hour. The solution was cooled to room temperature, and 20 mL of 1:1 hexane:ethyl acetate was added. The resultant white solid was collected by filtration to give 1.96 g (33%) of the title product. The filtrate was concentrated in vacuo and purified by flash chromatography eluting with 3:1 hexane:ethyl acetate to provide an additional 257 mg (4%) of pure 4-ethylamino-2-phenylamino-pyrimidine-5-carboxylic acid ethyl ester, mp 145-147°C.

Analysis calculated for $C_{15}H_{18}N_4O_2$: C, 62.92; H, 6.34; N, 19.57.

Found: C, 62.83; H, 6.24; N, 19.50.

EXAMPLE 6

(4-Ethylamino-2-phenylamino-pyrimidin-5-yl)-methanol

A solution of 4-ethylamino-2-phenylamino-pyrimidine-5-carboxylic acid ethyl ester (109 mg, 0.38 mmol) in 6 mL of tetrahydrofuran was added dropwise to a room temperature suspension of lithium aluminum hydride (35 mg, 0.92 mmol) in 5 mL of tetrahydrofuran. After 25 minutes, an additional 30 mg of lithium aluminum hydride was added, and stirring was continued for 30 minutes. The reaction was carefully quenched with 120 μL of water, 200 μL of 15% NaOH, and an additional 300 μL of water. After stirring for 1 hour, the white precipitate was removed by filtration, washing with ethyl acetate. The filtrate was concentrated in vacuo, and the crude material was purified by flash chromatography eluting with ethyl acetate to provide 36 mg (39%) of (4-ethylamino-2-phenylamino-pyrimidin-5-yl)-methanol, mp 174-176°C.

Analysis calculated for $C_{13}H_{16}N_4O$: C, 63.92; H, 6.60; N, 22.93.

Found: C, 63.97; H, 6.58; N, 22.79.

EXAMPLE 7

4-Ethylamino-2-phenylamino-pyrimidine-5-carboxaldehyde

To a solution of (4-ethylamino-2-phenylamino-pyrimidin-5-yl)-methanol (173 mg, 0.71 mmol) in 15 mL of chloroform was added manganese oxide (600 mg, 6.89 mmol). After stirring at room temperature overnight, the mixture was filtered through a pad of celite, washing with chloroform. The filtrate was concentrated in vacuo to give 170 mg (99%) of 4-ethylamino-2-phenylamino-pyrimidine-5-carboxaldehyde, mp 155-157°C.

Analysis calculated for $C_{13}H_{14}N_4O$: C, 64.45; H, 5.82; N, 23.12.

Found: C, 64.31; H, 6.01; N, 22.98.

EXAMPLE 8

4-Methylamino-2-methanesulfanyl-pyrimidine-5-carboxylic acid ethyl ester

To a room temperature solution of 4-chloro-2-methanesulfanyl-pyrimidine-5-carboxylic acid ethyl ester (18.66 g , 80.4 mmol) in 260 mL of tetrahydrofuran was added triethylamine (34 mL, 244 mmol) followed by 30 mL of a 40% aqueous solution of methylamine. The solution was stirred for 30 minutes, then was concentrated in vacuo and partitioned between chloroform and saturated aqueous sodium bicarbonate. The organic layer was washed with brine, dried over magnesium sulfate, filtered, and concentrated to provide a white solid. The solid was suspended in hexane and filtered to provide 14.70 g (81%) of 4-methylamino-2-methanesulfanyl-pyrimidine-5-carboxylic acid ethyl ester, mp 91-93°C. Literature mp 93-94°C: *J. Org. Chem.*, 1960:2137.

Analysis calculated for $C_9H_{13}N_3O_2S$: C, 47.56; H, 5.76; N, 18.49.

Found: C, 47.93; H, 5.67; N, 18.58.

EXAMPLE 9

(4-Methylamino-2-methanesulfanyl-pyrimidin-5-yl)-methanol

A solution of 4-methylamino-2-methanesulfanyl-pyrimidine-5-carboxylic acid ethyl ester (4.36 g, 19.3 mmol) in 60 mL of tetrahydrofuran was added dropwise to a room temperature suspension of lithium aluminum hydride (1.10 g, 29.0 mmol) in 40 mL of tetrahydrofuran. After 10 minutes, the reaction was carefully quenched with 2 mL of water, 2 mL of 15% NaOH, and 7 mL of water,

and the mixture was stirred for 1 hour. The white precipitate was removed by filtration, washing with ethyl acetate. The filtrate was concentrated in vacuo and 25 mL of 3:1 hexane:ethyl acetate was added. The solids were collected to give 2.99 g (84%) of (4-methylamino-2-methanesulfanyl-pyrimidin-5-yl) methanol, mp 155-157°C. Literature, mp 157-159°C: *J. Chem. Soc.*, 1968:733.

Analysis calculated for $C_7H_{11}N_3OS$: C, 45.39; H, 5.99; N, 22.68.

Found: C, 45.42; H, 5.93; N, 22.42.

EXAMPLE 10

4-Methylamino-2-methanesulfanyl-pyrimidine5-carboxaldehyde

To (4-methylamino-2-methanesulfanyl-pyrimidin-5-yl)-methanol (5.78 g, 31.2 mmol) in 600 mL of chloroform was added manganese oxide (25.0 g, 286 mmol). The suspension was stirred at room temperature for 6 hours then filtered through celite washing with 300 mL of chloroform. The filtrate was concentrated in vacuo, and hexane was added to the residue. The solid was collected to give 5.35 g (93%) of 4-methylamino-2-methanesulfanyl-pyrimidine-5-carboxaldehyde, mp 97-100°C.

EXAMPLE 11

4-Amino-2-methanesulfanyl-pyrimidine-5-carboxylic acid ethyl ester

To a room temperature solution of 4-chloro-2-methanesulfanyl-pyrimidine-5-carboxylic acid ethyl ester (15.0 g , 65 mmol) in 200 mL of tetrahydrofuran was added 25 mL of triethylamine followed by 35 mL of aqueous ammonium hydroxide. After stirring at room temperature for 1.5 hours, an additional 30 mL of aqueous ammonium hydroxide was added, and stirring was continued for 1 hour. The reaction mixture was concentrated in vacuo and partitioned between ethyl acetate and saturated aqueous sodium bicarbonate. The organic layer was washed with brine, dried over magnesium sulfate, filtered, and concentrated in vacuo. Ethyl acetate and hexane were added, and the resultant solid was collected by filtration to provide 10.84 g (79%) of 4-amino-2-methanesulfanyl-pyrimidine-5-carboxylic acid ethyl ester.

EXAMPLE 12

(4-Amino-2-methanesulfanyl-pyrimidin-5-yl)-methanol

A solution of 4-amino-2-methanesulfanyl-pyrimidine-5-carboxylic acid ethyl ester (13.36 g, 63 mmol) in 250 mL of tetrahydrofuran was added dropwise to a room temperature suspension of lithium aluminum hydride (3.82 g, 100 mmol) in 250 mL of tetrahydrofuran. After 30 minutes, the reaction was cooled to 0°C, and isopropyl alcohol was added until bubbling diminished. The reaction was quenched with 15 mL of water, 15 mL of 15% NaOH, and 50 mL of water, and the mixture was stirred for 1 hour. The white precipitate was removed by filtration, washing with ethyl acetate. The filtrate was concentrated in vacuo and 3:1 hexane:ethyl acetate was added. The solids were collected, washed with 3:1 hexane:ethyl acetate, followed by hexane. The solid was dissolved in ethyl acetate, and the solution was dried over magnesium sulfate. Filtration followed by concentration in vacuo gave 8.14 g (76%) of (4-amino-2-methanesulfanyl-pyrimidin-5-yl)-methanol.

Analysis calculated for $C_6H_9N_3OS$: C, 42.09; H, 5.30; N, 24.54.

Found: C, 42.31; H, 5.24; N, 24.27.

EXAMPLE 13

4-Amino-2-methanesulfanyl-pyrimidine-5-carboxaldehyde

To (4-amino-2-methanesulfanyl-pyrimidin-5-yl)-methanol (8.14 g, 48 mmol) in 1 L of chloroform was added manganese oxide (33.13 g, 381 mmol). The suspension was stirred at room temperature overnight then filtered through celite washing with 300 mL of chloroform. The filtrate was concentrated in vacuo to give 8.14 g (quantitative yield) of 4-amino-2-methanesulfanyl-pyrimidine-5-carboxaldehyde, mp 185-187°C. Literature mp = 183-184°C, *JOC*, 1958;23:1738.

Analysis calculated for $C_6H_7N_3OS$: C, 42.59; H, 4.17; N, 24.83.

Found: C, 42.84; H, 4.21; N, 24.73.

EXAMPLE 14

4-(4-Methoxybenzylamino)-2-methanesulfanyl-pyrimidine-5-carboxylic acid ethyl ester

To a room temperature solution of 4-chloro-2-methanesulfanyl-pyrimidine-5-carboxylic acid ethyl ester (6.05 g , 26.07 mmol) in 60 mL of tetrahydrofuran was added triethylamine (11 mL, 79.5 mmol) followed by 3.6 mL (27.6 mmol) of 4-methoxybenzylamine. The solution was stirred for 1 hour then filtered. The white solid was washed with ethyl acetate, and the filtrate was concentrated in vacuo. The residue was partitioned between chloroform and saturated aqueous sodium bicarbonate. The organic layer was dried over magnesium sulfate, filtered, and concentrated to provide 7.60 g (88%) of 4-(4-methoxybenzylamino)-2-methanesulfanyl-pyrimidine-5-carboxylic acid ethyl ester, mp 72-74°C.

Analysis calculated for $C_{16}H_{19}N_3O_3S$: C, 57.64; H, 5.74; N, 12.60.

Found: C, 57.65; H, 5.80; N, 12.57.

EXAMPLE 15

[4-(4-Methoxybenzylamino)-2-methanesulfanyl-pyrimidin-5-yl]-methanol

A solution of 4-(4-methoxybenzylamino)-2-methanesulfanyl-pyrimidine-5-carboxylic acid ethyl ester (6.89 g, 20.70 mmol) in 60 mL of tetrahydrofuran was added dropwise to a room temperature suspension of lithium aluminum hydride (1.17 g, 30.8 mmol) in 40 mL of tetrahydrofuran. After 30 minutes, the reaction was carefully quenched with 2 mL of water, 2 mL of 15% NaOH, and 7 mL of water, and the mixture was stirred to give a white precipitate. The solid was removed by filtration, washing with ethyl acetate. The filtrate was partially concentrated in vacuo, and the white solid was collected by filtration to give 1.47 g (24%) of product. The filtrate was concentrated, and upon addition of 3:1 hexane:ethyl acetate, additional solid formed. The precipitate was collected to give 3.16 g (52%) of [4-(4-methoxybenzylamino)-2-methanesulfanyl-pyrimidin-5-yl]-methanol, mp 163-165°C.

Analysis calculated for $C_{14}H_{17}N_3O_2S$: C, 57.71; H, 5.88; N, 14.42.

Found: C, 57.78; H, 5.88; N, 14.36.

EXAMPLE 16

4-(4-Methoxybenzylamino)-2-methanesulfanyl-pyrimidine-5-carboxaldehyde

To [4-(4-methoxybenzylamino)-2-methanesulfanyl-pyrimidin-5-yl]-methanol (4.08 g, 14.02 mmol) in 400 mL of chloroform was added manganese oxide (10.90 g, 125 mmol). The suspension was stirred at room temperature for 8 hours and then filtered through celite washing with chloroform. The filtrate was concentrated in vacuo followed by the addition of hexane to give 3.87 g (96%) of 4-(4-methoxybenzylamino)-2-methanesulfanyl-pyrimidine-5-carboxaldehyde, mp 87-89°C.

Analysis calculated for $C_{14}H_{15}N_3O_2S$: C, 58.11; H, 5.23; N, 14.52.

Found: C, 57.88; H, 5.12; N, 14.35.

EXAMPLE 17

Ethyl 3-(4-Ethylamino-2-phenylamino-pyrimidin-5-yl)acrylate

To a room temperature solution of 4-ethylamino-2-phenylamino-pyrimidine-5-carboxaldehyde (320 mg, 1.32 mmol) in 12 mL of tetrahydrofuran was added (carbethoxymethylene)triphenylphosphorane (720 mg, 2.07 mmol). The reaction mixture was heated at reflux for 7 hours then stirred at room temperature overnight. An additional amount of (carbethoxymethylene)triphenylphosphorane (300 mg, 0.86 mmol) was added, and the reaction mixture was heated at reflux for an additional 8 hours then stirred at room temperature for 3 days. The reaction mixture was concentrated in vacuo, and the residue was purified by flash chromatography, eluting with 1:2 ethyl acetate:hexane, to provide 357 mg (86%) of ethyl 3-(4-ethylamino-2-phenylamino-pyrimidin-5-yl)acrylate, mp 125-126°C.

Analysis calculated for $C_{17}H_{20}N_4O_2$: C, 65.37; H, 6.45; N, 17.94.

Found: C, 65.40; H, 6.57; N, 17.64.

EXAMPLE 18

8-Ethyl-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one

To a room temperature solution of ethyl 3-(4-ethylamino-2-phenylamino pyrimidin-5-yl)acrylate (179 mg, 0.57 mmol) in 10 mL of triethylamine was added 90 μL of 1,8-diazabicyclo[5.4.0]undec-7-ene. The reaction mixture was

heated at reflux for 8.5 hours then stirred at room temperature overnight. An additional amount of 1,8-diazabicyclo[5.4.0]undec-7-ene (90 μL) was added, and the reaction mixture was heated at reflux for 9 hours then stirred at room temperature overnight. The reaction mixture was concentrated in vacuo and purified by flash chromatography, followed by recrystallization from ethyl acetate:hexane, to provide 8-ethyl-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one, mp 203-204°C.

Analysis calculated for $C_{15}H_{14}N_4O$ 0.05 EtOAc: C, 67.45; H, 5.36; N, 20.70.

Found: C, 67.29; H, 5.40; N, 20.62.

EXAMPLE 19

Ethyl 3-(4-Amino-2-methanesulfanyl-pyrimidin-5-yl)acrylate

To a room temperature solution of 4-amino-2-methanesulfanyl-pyrimidine-5-carbaldeyde (4.08 g, 24.14 mmol) in 100 mL of tetrahydrofuran was added (carbethoxymethylene)triphenylphosphorane (10.80 g, 31 mmol). The reaction mixture was heated at reflux for 3 hours then stirred at room temperature overnight. The reaction mixture was concentrated in vacuo, and the residue was purified by flash chromatography, eluting with 1:1 ethyl acetate:hexane, to provide 4.30 g (75%) of ethyl 3-(4-amino-2-methanesulfanyl-pyrimidin-5-yl)acrylate, mp softens at 108°C.

Analysis calculated for $C_{10}H_{13}N_3O_2S$: C, 50.19; H, 5.48; N, 17.56.

Found: C, 50.22; H, 5.45; N, 17.24.

EXAMPLE 20

2-Methanesulfanyl-8H-pyrido[2,3-d]pyrimidin-7-one

To a room temperature solution of ethyl 3-(4-amino-2-methanesulfanyl pyrimidin-5-yl)acrylate (368 mg, 1.53 mmol) in 3 mL of N,N-diisopropylethylamine was added 380 μL of 1,8-diazabicyclo[5.4.0]undec-7-ene. The reaction mixture was heated at reflux for 3 hours then cooled to room temperature and concentrated. The residue was purified by flash chromatography eluting with ethyl acetate. The fractions containing the product were partially concentrated in vacuo, and the solids were removed by filtration to provide

134 mg (45%) of 2-methanesulfanyl-8H-pyrido[2,3-d]pyrimidin-7-one, mp 269-271°C.

Analysis calculated for $C_8H_7N_3OS$: C, 49.73; H, 3.65; N, 21.75.

Found: C, 49.67; H, 3.46; N, 21.49.

EXAMPLE 21

8-Ethyl-2-methanesulfanyl-8H-pyrido[2,3-d]pyrimidin-7-one

To a suspension of NaH (80 mg of a 60% suspension of NaH in mineral oil) in 10 mL of dimethylformamide was added 2-methanesulfanyl-8H-pyrido[2,3-d]pyrimidin-7-one (262 mg, 1.35 mmol). The reaction mixture was heated to 50°C resulting in a brown solution. The solution was cooled slightly and iodoethane (150 μL, 1.88 mmol) was added. The reaction was heated at 50°C for 10 minutes, then cooled to room temperature and partitioned between cold water and ethyl acetate. The organic layer was dried over magnesium sulfate, filtered, and concentrated in vacuo. The residue was purified by flash chromatography, eluting with 1:1 ethyl acetate:hexane to all ethyl acetate, to provide 192 mg (64%) of 8-ethyl-2-methanesulfanyl-8H-pyrido[2,3-d]pyrimidin-7-one, mp 104-106°C.

Analysis calculated for $C_{10}H_{11}N_3OS$: C, 54.28; H, 5.01; N, 18.99.

Found: C, 54.28; H, 5.03; N, 19.06.

Alternate Preparation of Example 21

8-Ethyl-2-methanesulfanyl-8H-pyrido[2,3-d]pyrimidin-7-one

To a room temperature solution of ethyl 3-(4-ethylamino-2-methanesulfanyl-pyrimidin-5-yl)acrylate (6.62 g, 24.78 mmol) in 30 mL of N,N-diisopropylethylamine was added 4.25 mL of 1,8-diazabicyclo[5.4.0]undec-7-ene. The reaction mixture was heated at reflux overnight then cooled to room temperature. The resultant solid was collected by filtration and washed with 1:1 hexane:ethyl acetate to give 1.83 g (33%) of 8-ethyl-2-methanesulfanyl-8H-pyrido[2,3-d]pyrimidin-7-one. The filtrate was concentrated in vacuo and upon the addition of hexane, a solid formed that was collected, washed with hexane, and purified by flash chromatography eluting with ethyl acetate to provide an additional 2.22 g (40%) of title product.

EXAMPLE 22

8-Ethyl-2-methanesulfinyl-8H-pyrido[2,3-d]pyrimidin-7-one

To a room temperature solution of 8-ethyl-2-methanesulfanyl-8H-pyrido[2,3-d]pyrimidin-7-one (2.22 g, 10.04 mmol) in 100 mL of chloroform was added (±)-*trans*-2-(phenylsulfonyl)-3-phenyloxaziridine (3.17 g, 12.15 mmol). The solution was stirred at room temperature overnight then concentrated in vacuo. The residue was treated with ethyl acetate to give a solid that was collected by filtration and washed with ethyl acetate to provide 2.21 g (93%) of 8-ethyl-2-methanesulfinyl-8H-pyrido[2,3-d]pyrimidin-7-one, mp 202-203°C. Analysis calculated for $C_{10}H_{11}N_3O_2S$: C, 50.62; H, 4.67; N, 17.71. Found: C, 50.30; H, 4.54; N, 17.45.

EXAMPLE 23

8-Ethyl-2-methanesulfonyl-8H-pyrido[2,3-d]pyrimidin-7-one

To a room temperature solution of 8-ethyl-2-methanesulfanyl-8H-pyrido[2,3-d]pyrimidin-7-one (328 mg, 1.48 mmol) in 15 mL of chloroform was added *m*-chloroperbenzoic acid (*m*-CPBA) (810 mg of 50%-60% *m*-CPBA, remainder water). The reaction was stirred at room temperature for 1.5 hours then partitioned between chloroform and saturated sodium bicarbonate. The organic layer was dried over magnesium sulfate, filtered, and concentrated in vacuo. The residue was purified by flash chromatography, eluting with a gradient of ethyl acetate to 10% methanol in ethyl acetate, to provide 147 mg (39%) of product that contained trace amounts of impurities, and 42 mg (11%) of analytically pure 8-ethyl-2-methanesulfonyl-8H-pyrido[2,3-d]pyrimidin-7-one, mp 184-186°C. Analysis calculated for $C_{10}H_{11}N_3O_3S$ $0.25H_2O$: C, 46.59; H, 4.50; N, 16.30. Found: C, 46.77; H, 4.44; N, 16.24.

EXAMPLE 24

Ethyl 3-(4-Ethylamino-2-methanesulfanyl-pyrimidin-5-yl)acrylate

To a room temperature solution of 4-ethylamino-2-methanesulfanyl-pyrimidine-5-carboxaldehyde (6.34 g, 32.14 mmol) in 100 mL of tetrahydrofuran was added (carbethoxymethylene)triphenylphosphorane (14.32 g, 41.14 mmol). The reaction mixture was heated at reflux for 70 minutes then concentrated

in vacuo and the residue partitioned between ethyl acetate and 1N HCl. The organic layer was extracted with additional 1N HCl, the acidic layers were combined and treated with saturated sodium bicarbonate until basic. The product was extracted into ethyl acetate, and the organic layer was dried over magnesium sulfate, filtered, and concentrated. Upon the addition of hexane, a solid formed. The solid was collected by filtration to give 6.79 g (79%) of ethyl 3-(4-ethylamino-2-methanesulfanyl-pyrimidin-5-yl)acrylate. An analytical sample was obtained by flash chromatography eluting with ethyl acetate, mp 79-80°C.

Analysis calculated for $C_{12}H_{17}N_3O_2S$: C, 53.91; H, 6.41; N, 15.72.

Found: C, 53.97; H, 6.52; N, 15.78.

EXAMPLE 25

Ethyl 3-(4-Methylamino-2-methanesulfanyl-pyrimidin-5-yl)acrylate

To a room temperature solution of 4-methylamino-2-methanesulfanyl pyrimidine-5-carboxaldehyde (5.00 g, 27.30 mmol) in 90 mL of tetrahydrofuran was added (carbethoxymethylene)triphenylphosphorane (12.35 g, 35.49 mmol). The reaction mixture was heated at reflux for 2.5 hours then cooled to room temperature and concentrated in vacuo. The residue was partitioned between ethyl acetate and 1N HCl. The organic layer was treated with saturated sodium bicarbonate until basic. The product was extracted into ethyl acetate and the organic layer dried over magnesium sulfate, filtered, and concentrated. Upon the addition of 4:1 hexane:ethyl acetate, a solid formed that was collected by filtration to give 5.76 g (83%) of ethyl 3-(4 methylamino-2-methanesulfanyl-pyrimidin-5-yl)acrylate, mp 142-144°C.

Analysis calculated for $C_{11}H_{15}N_3O_2S$: C, 52.16; H, 5.97; N, 16.59.

Found: C, 51.89; H, 5.87; N, 16.38.

EXAMPLE 26

8-Methyl-2-methanesulfanyl-8H-pyrido[2,3-d]pyrimidin-7-one

To a room temperature solution of ethyl 3-(4-methylamino-2-methanesulfanyl-pyrimidin-5-yl)acrylate (1.14 g, 4.48 mmol) in 6 mL of N,N-diisopropylethylamine was added 700 µL of 1,8-diazabicyclo[5.4.0]undec-7-ene. The reaction mixture was heated at reflux overnight then cooled to room

temperature. An additional amount of 1,8-diazabicyclo[5.4.0]undec-7-ene (700 μL) was added, and the mixture was heated at reflux for 5 hours. The mixture was cooled to room temperature, and the solid was removed by filtration and purified by flash chromatography eluting with ethyl acetate. The fractions were concentrated and upon the addition of 3:1 hexane:ethyl acetate, a solid formed and was collected providing 172 mg (18%) of pure 8-methyl-2-methanesulfanyl-8H-pyrido[2,3-d]pyrimidin-7-one. Concentration of the filtrate provided an additional 184 mg (20%) of product, mp 190-192°C.

Analysis calculated for $C_9H_9N_3OS$: C, 52.16; H, 4.38; N, 20.27.

Found: C, 52.03; H, 4.24; N, 20.15.

EXAMPLE 27

8-Methyl-2-methanesulfonyl-8H-pyrido[2,3-d]pyrimidin-7-one

To a room temperature solution of 8-methyl-2-methanesulfanyl-8H-pyrido[2,3-d]pyrimidin-7-one (187 mg, 0.90 mmol) in 10 mL of chloroform was added *m*-CPBA (550 mg of 50%-60% *m*-CPBA, remainder water). The reaction was stirred at room temperature for 2 hours then partitioned between chloroform and saturated sodium bicarbonate. The organic layer was dried over magnesium sulfate, filtered, and concentrated in vacuo. Upon the addition of chloroform followed by hexane, a solid formed and was collected to give 144 mg (67%) of 8-methyl-2-methanesulfonyl-8H-pyrido[2,3-d]pyrimidin-7-one, mp 194-196°C.

Analysis calculated for $C_9H_9N_3O_3S$: C, 45.18; H, 3.79; N, 17.56.

Found: C, 44.98; H, 3.76; N, 17.38.

EXAMPLE 28

Ethyl 3-(4-Amino-2-phenylamino-pyrimidin-5-yl)acrylate

To a 0°C solution of 4-amino-2-phenylamino-pyrimidine-5-carbonitrile (7.00 g, 33.18 mmol) (literature prep: *J. Org. Chem.*, 1960:5711) in 170 mL of tetrahydrofuran was added 45 mL of a 1 M solution of diisobutylaluminum hydride in methylene chloride. The ice bath was removed, and an additional 40 mL of a 1 M solution of diisobutylaluminum hydride in methylene chloride was added. The reaction mixture was cooled to 0°C, and 60 mL of methanol was

added dropwise. This mixture was then added to a rapidly stirring mixture of 300 mL of ethyl acetate and 250 mL of 1N HCl. The layers were separated, and the organic layer was extracted with additional 1N HCl. The acid layers were combined, treated with 330 mL of 1N NaOH, and extracted with ethyl acetate. The organic layer was dried over magnesium sulfate, filtered, and concentrated. Purification by flash chromatography eluting with ethyl acetate gave 4.99 g (68%) of 4-amino-2-phenylamino-pyrimidine-5-carboxaldehyde.

To a room temperature solution of 4-amino-2-phenylamino-pyrimidine-5-carboxaldehyde (2.89 g, 13.50 mmol) in 120 mL of tetrahydrofuran was added (carbethoxymethylene)triphenylphosphorane (11.00 g, 31.60 mmol). The reaction mixture was heated at reflux for 9 hours then stirred at room temperature overnight. The solution was concentrated in vacuo and treated with ethyl acetate and hexane to give a yellow solid. The solid was collected by filtration and purified by flash chromatography to give 1.55 g (40%) of ethyl 3-(4-amino-2-phenylamino-pyrimidin-5-yl)acrylate, mp 190-192°C.

Analysis calculated for $C_{15}H_{16}N_4O_2$: C, 63.37; H, 5.67; N, 19.71.

Found: C, 63.08; H, 5.72; N, 19.72.

EXAMPLE 29

8-(4-Methoxybenzylamino)-2-methanesulfanyl-8H-pyrido[2,3-d]pyrimidin-7-one

To a room temperature solution of 4-(4-methoxybenzylamino)-2-methanesulfanyl-pyrimidine-5-carboxaldehyde (1.35 g, 4.65 mmol) in 25 mL of tetrahydrofuran was added (carbethoxymethylene)triphenylphosphorane (2.10 g, 6.00 mmol). The reaction mixture was heated at reflux for 6 hours then stirred at room temperature for 3 days. The reaction mixture was concentrated in vacuo and the residue partitioned between ethyl acetate and 1N HCl. The acidic layer was treated with saturated sodium bicarbonate until basic. The product was extracted into ethyl acetate, and the organic layer was dried over magnesium sulfate. Filtration, concentration, and purification by flash chromatography eluting with 1:2 ethyl acetate:hexane provided 1.22 g (73%) of ethyl 3-(4-(4-methoxybenzylamino)-2-methanesulfanyl-pyrimidin-5-yl)acrylate as a thick oil.

To a room temperature solution of ethyl 3-(4-(4-methoxybenzylamino)-2-methanesulfanyl-pyrimidin-5-yl)acrylate (950 mg, 2.65 mmol) in 10 mL of N,N-diisopropylethylamine was added 3.4 mL of 1,8-diazabicyclo[5.4.0]undec-7-ene. The reaction mixture was heated at reflux for 4.5 hours then stirred at room temperature overnight. The liquid was decanted from the gummy solid and ethyl acetate was added to the residue. The solid was collected by filtration and washed with methanol to provide 141 mg (17%) of product. The filtrate was concentrated, and methanol was added. The solid was removed by filtration to provide 240 mg of analytically pure 8-(4-methoxybenzylamino)-2-methanesulfanyl-8H-pyrido[2,3-d]pyrimidin-7-one (28%). The filtrate was concentrated and purified by flash chromatography eluting with ethyl acetate to provide an additional 162 mg (19%) of product, mp 160-162°C.

Analysis calculated for $C_{16}H_{15}N_3O_2S$: C, 61.32; H, 4.82; N, 13.41.

Found: C, 61.06; H, 4.78; N, 13.47.

EXAMPLE 30

2-Methanesulfinyl-8H-pyrido[2,3-d]pyrimidin-7-one

To a room temperature solution of 2-methanesulfanyl-8H-pyrido[2,3-d]pyrimidin-7-one (120 mg, 0.62 mmol) in 20 mL of chloroform was added (±)-*trans*-2-(phenylsulfonyl)-3-phenyloxaziridine (200 mg, 0.77 mmol). The solution was stirred at room temperature overnight. The solid was collected by filtration and found to be 2-methylthio-8H-pyrido[2,3-d]pyrimidin-7-one. The filtrate was stirred at room temperature for 2 days then concentrated. Addition of ethyl acetate resulted in the formation of a solid that was collected by filtration to provide 64 mg (76% based on recovered starting material) of 2-methanesulfinyl-8H-pyrido[2,3-d]pyrimidin-7-one, mp 237-242°C.

Analysis calculated for $C_8H_7N_3O_2S$ $0.2H_2O$: C, 45.15; H, 3.50; N, 19.74.

Found: C, 45.41; H, 3.23; N, 19.80.

EXAMPLE 31

Mixture of 2-methanesulfinyl-8H-pyrido[2,3-d]pyrimidin-7-one and 2-methanesulfonyl 8H-pyrido[2,3-d]pyrimidin-7-one

To a room temperature suspension of 2-methanesulfanyl-8H-pyrido[2,3-d]pyrimidin-7-one (860 mg, 4.45 mmol) in 150 mL of chloroform was added *m*-CPBA (2.85 g of 50%-60% *m*-CPBA, remainder water). The reaction mixture was stirred at room temperature for 2 hours. The solid was filtered and washed with chloroform to give 924 mg of a mixture of 2-methanesulfinyl-8H-pyrido[2,3-d]pyrimidin-7-one and 2-methanesulfonyl-8H-pyrido[2,3-d]pyrimidin-7-one.

EXAMPLE 32

2-Phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one

A suspension of 204 mg of the mixture of 2-methanesulfinyl-8H-pyrido[2,3-d]pyrimidin-7-one and 2-methanesulfonyl-8H-pyrido[2,3-d]pyrimidin-7-one in 1 mL of aniline was heated at reflux for 10 minutes resulting in a dark brown solution. Upon cooling to room temperature, a solid formed. Ethyl acetate was added, and the solid was collected by filtration, washed with ethyl acetate, then suspended in methanol and filtered, and washed with additional methanol to provide 175 mg of 2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one, mp >350°C. Analysis calculated for $C_{13}H_{10}N_4S$ $0.15H_2O$: C, 64.80; H, 4.31; N, 23.25. Found: C, 64.56; H, 4.15; N, 23.59.

EXAMPLE 33

8-Isopropyl-2-methanesulfanyl-8H-pyrido[2,3-d]pyrimidin-7-one

To a suspension of NaH (48 mg of a 60% suspension of NaH in mineral oil) in 6 mL of dimethylformamide was added 2-methanesulfanyl-8H-pyrido[2,3-d]pyrimidin-7-one (158 mg, 0.82 mmol). The reaction mixture was heated to 50°C resulting in a yellow solution. The solution was cooled slightly and 2-iodopropane (120 μL, 1.20 mmol) was added. The reaction was heated at 50°C for 30 minutes then cooled to room temperature and partitioned between water and ethyl acetate. The organic layer was dried over magnesium sulfate, filtered, and concentrated in vacuo. The residue was purified by flash chromatography, eluting with a gradient of 1:3 ethyl acetate:hexane to all ethyl acetate, to provide 140 mg (69%) of 8-isopropyl-2-methanesulfanyl-8H-pyrido[2,3-d]pyrimidin-7-one, mp 101-102°C.

Analysis calculated for $C_{11}H_{13}N_3OS$: C, 56.15; H, 5.57; N, 17.86.

Found: C, 56.07; H, 5.59; N, 17.78.

EXAMPLE 34

8-Isopropyl-2-methanesulfinyl-8H-pyrido[2,3-d]pyrimidin-7-one

To a room temperature solution of 8-isopropyl-2-methanesulfanyl-8H-pyrido[2,3-d]pyrimidin-7-one (1.19 g, 5.08 mmol) in 50 mL of chloroform was added (±)-*trans*-2-(phenylsulfonyl)-3-phenyloxaziridine (1.76 g, 6.75 mmol). The solution was stirred at room temperature overnight then concentrated in vacuo. The residue was treated with ethyl acetate and hexane to give a solid which was collected by filtration and purified by flash chromatography, eluting with a gradient of ethyl acetate to 10% methanol in ethyl acetate, to provide 1.00 g (78%) of 8-isopropyl-2-methanesulfinyl-8H-pyrido[2,3-d]pyrimidin-7-one, mp 132-133°C.

Analysis calculated for $C_{11}H_{13}N_3O_2S$: C, 52.57; H, 5.21; N, 16.72.

Found: C, 52.68; H, 5.24; N, 16.48.

EXAMPLES 35-43

General procedure for the preparation of 8-substituted-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-ones from 2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one

Used to prepare EXAMPLES 35-43

To a suspension of NaH (1.0-1.5 equivalents of a 60% suspension of NaH in mineral oil) in 5 mL of dimethylformamide was added 2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one (1 equivalent). The reaction mixture was heated to 50°C to 60°C resulting in a yellow solution. The solution was cooled slightly and the desired alkyl halide (1.1-2.0 equivalents) was added. The reaction mixture was heated at 50°C, for a time ranging from 5 minutes to 1 hour, then cooled to room temperature and partitioned between water and ethyl acetate. In some cases, the organic layer was washed with additional water or brine. The organic layer was dried over magnesium sulfate, filtered, and concentrated in vacuo. The residue was purified by the procedure noted.

EXAMPLE 35

8-Benzyl-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one

Purified by flash chromatography eluting with a gradient of 1:1 ethyl acetate:hexane to all ethyl acetate (35%), mp 215-216°C.

Analysis calculated for $C_{20}H_{16}N_4O$: C, 72.16; H, 5.00; N, 16.83.

Found: C, 72.45; H, 4.83; N, 16.88.

EXAMPLE 36

7-Oxo-2-phenylamino-7H-pyrido[2,3-d]pyrimidin-8-yl)-acetic acid methyl ester

Purified by adding methanol and ethyl acetate to the residue and collecting the resultant solid (44%), mp 232-233°C.

Analysis calculated for $C_{16}H_{14}N_4O_3$: C, 61.93; H, 4.55; N, 18.05.

Found: C, 61.68; H, 4.53; N, 18.02.

EXAMPLE 37

8-Methoxymethyl-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one

Purified by flash chromatography eluting with a gradient of 1:1 ethyl acetate:hexane to all ethyl acetate (61%), mp 173-174°C.

Analysis calculated for $C_{15}H_{14}N_4O_2$: C, 63.82; H, 5.00; N, 19.85.

Found: C, 63.60; H, 4.86; N, 19.59.

EXAMPLE 38

8-(3-Benzyloxypropyl)-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one

Purified by flash chromatography eluting with a gradient of 1:1 ethyl acetate:hexane to all ethyl acetate (46%), mp 133-135°C.

Analysis calculated for $C_{23}H_{22}N_4O_2$: C, 71.48; H, 5.74; N, 14.50.

Found: C, 71.20; H, 5.67; N, 14.35.

EXAMPLE 39

8-Oxiranylmethyl-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one

Purified by flash chromatography eluting with a gradient of 1:1 ethyl acetate:hexane to all ethyl acetate to 10% methanol in ethyl acetate (38%), mp 163-165°C.

Analysis calculated for $C_{16}H_{14}N_4O_2$ 0.05 $CH_3COOCH_2CH_3$: C, 65.13; H, 4.86; N, 18.76. Found: C, 64.73; H, 4.76; N, 18.66.

EXAMPLE 40

8-Butyl-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one

Purified by flash chromatography eluting with a gradient of 1:1 ethyl acetate:hexane to all ethyl acetate (42%), mp 183-184°C.

Analysis calculated for $C_{17}H_{18}N_4O$ 0.25 H_2O: C, 68.32; H, 6.24; N, 18.75. Found: C, 68.35; H, 5.97; N, 18.69.

EXAMPLE 41

2-Phenylamino-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one

Purified by flash chromatography eluting with a gradient of 1:1 ethyl acetate:hexane to all ethyl acetate (65%), mp 163-164°C.

Analysis calculated for $C_{16}H_{16}N_4O$: C, 68.55; H, 5.75; N, 19.99. Found: C, 68.56; H, 5.97; N, 19.73.

EXAMPLE 42

8-Isobutyl-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one

Purified by flash chromatography eluting with 1:1 ethyl acetate:hexane (72%), mp 170-171°C.

Analysis calculated for $C_{17}H_{18}N_4O$ 0.05 $CH_3COOCH_2CH_3$: C, 68.89; H, 6.31; N, 18.47. Found: C, 68.60; H, 6.20; N, 18.15.

EXAMPLE 43

8-Isopropyl-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one

Purified by flash chromatography eluting with a gradient of 1:1 ethyl acetate:hexane to all ethyl acetate (23%), mp 170-171°C.

Analysis calculated for $C_{16}H_{16}N_4O$: C, 68.55; H, 5.75; N, 19.99.

Found: C, 68.31; H, 5.73; N, 19.88.

EXAMPLES 44-45

General procedure for the preparation of 2-amino-8-ethyl-8H-pyrido[2,3-d]pyrimidin-7-ones from 8-ethyl-2-methanesulfonyl-8H-pyrido[2,3-d]pyrimidin-7-one

Used to prepare EXAMPLES 44-45

To 8-ethyl-2-methanesulfonyl-8H-pyrido[2,3-d]pyrimidin-7-one (1 equivalent) was added 1 to 10 equivalents of an amine. In those examples where the amine used was aniline or a substituted aniline, the reaction mixture was heated at 175°C for 10 minutes to 1 hour. In the case of primary amines, the reaction was run at room temperature for 10 to 60 minutes. The reaction mixture was partitioned between saturated sodium bicarbonate and ethyl acetate. In some cases, the organic layer was washed with additional water or brine. The organic layer was dried over magnesium sulfate, filtered, and concentrated in vacuo. The residue was purified by the procedure noted.

Alternate preparation of EXAMPLE 18

8-Ethyl-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one

Purified by flash chromatography eluting with a gradient of 1:1 hexane: ethyl acetate to all ethyl acetate (40%), mp 194-195°C.

Analysis calculated for $C_{15}H_{14}N_4O$: C, 67.65; H, 5.30; N, 21.04.

Found: C, 67.34; H, 5.19; N, 20.88.

EXAMPLE 44

2-Benzylamino-8-ethyl-8H-pyrido[2,3-d]pyrimidin-7-one

Purified by adding 3:1 hexane:ethyl acetate to the residue and collecting the resultant solid (41%), mp 96-97°C.

Analysis calculated for $C_{16}H_{16}N_4O$: C, 68.55; H, 5.75; N, 19.99.

Found: C, 68.00; H, 5.87; N, 19.20.

EXAMPLE 45

8-Ethyl-2-ethylamino-8H-pyrido[2,3-d]pyrimidin-7-one

Analytical material was obtained directly (87%), mp 60-161°C.

Analysis calculated for $C_{11}H_{14}N_4O$: C, 60.53; H, 6.47; N, 25.67.

Found: C, 60.27; H, 6.35; N, 25.61.

EXAMPLES 46-54

General procedure for the preparation of 2-amino-8-ethyl-8H-pyrido[2,3-d]pyrimidin-7-ones from 8-ethyl-2-methanesulfinyl-8H-pyrido[2,3-d]pyrimidin-7-one

Used to prepare EXAMPLES 46-54

To 8-ethyl-2-methanesulfinyl-8H-pyrido[2,3-d]pyrimidin-7-one (1 equivalent) was added 1 to 10 equivalents of an amine. In those cases where the amine was aniline, a substituted aniline, or a tertiary amine, the reaction mixture was heated at 175°C for 10 minutes to 1 hour. In the case of primary or secondary alkyl amines, the reaction was run at room temperature for 10 to 60 minutes. The reaction mixture was worked up and purified by the procedure noted.

EXAMPLE 46

2-tert-Butylamino-8-ethyl-8H-pyrido[2,3-d]pyrimidin-7-one

After cooling to room temperature, the reaction mixture was partitioned between chloroform and saturated sodium bicarbonate. The organic layer was dried over magnesium sulfate, filtered, and concentrated in vacuo. The residue was purified by flash chromatography eluting with ethyl acetate (32%), mp 103-104°C.

Analysis calculated for $C_{13}H_{18}N_4O$ 0.25 H_2O: C, 62.27; H, 7.39; N, 22.36.

Found: C, 62.64; H, 7.45; N, 22.35.

EXAMPLE 47

8-Ethyl-2-isopropylamino-8H-pyrido[2,3-d]pyrimidin-7-one

The reaction mixture was partitioned between ethyl acetate and saturated sodium bicarbonate. The organic layer was dried over magnesium sulfate, filtered, and concentrated in vacuo (71%), mp 119-120°C.

Analysis calculated for $C_{12}H_{16}N_4O$: C, 62.05; H, 6.94; N, 24.12.

Found: C, 61.84; H, 7.04; N, 23.92.

EXAMPLE 48

2-Cyclohexylamino-8-ethyl-8H-pyrido[2,3-d]pyrimidin-7-one

The reaction mixture was partitioned between ethyl acetate and saturated sodium bicarbonate. The organic layer was washed with brine, dried over magnesium sulfate, filtered, and concentrated in vacuo. The solid was washed with hexane and filtered (67%), mp 135-136°C.

Analysis calculated for $C_{15}H_{20}N_4O$: C, 66.15; H, 7.40; N, 20.57.

Found: C, 66.20; H, 7.54; N, 20.57.

EXAMPLE 49

2-(Biphenyl-4-ylamino)-8-ethyl-8H-pyrido[2,3-d]pyrimidin-7-one

After cooling to room temperature, ethyl acetate and hexane were added, and the resultant solid was collected and purified by flash chromatography eluting with ethyl acetate. A second chromatography eluting with a gradient of 2:1 hexane:ethyl acetate to all ethyl acetate gave clean product (32%), mp 207-208°C.

Analysis calculated for $C_{21}H_{18}N_4O$ 0.5 H_2O: C, 71.79; H, 5.41; N, 15.95.

Found: C, 72.08; H, 5.35; N, 15.78.

EXAMPLE 50

8-Ethyl-2-(pyridin-4-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one

After cooling to room temperature, the reaction mixture was partitioned between chloroform and saturated sodium bicarbonate. The aqueous phase was extracted with additional chloroform, and the organic layers were combined, washed with brine, dried over magnesium sulfate, filtered, and concentrated in vacuo. The residue was purified by flash chromatography eluting with 5% chloroform in ethyl acetate (33%), mp 259-260°C.

Analysis calculated for $C_{14}H_{13}N_5O$ 0.25 H_2O: C, 61.87; H, 4.97; N, 25.78.

Found: C, 61.94; H, 4.73; N, 25.47.

EXAMPLE 51

8-Ethyl-2-(4-methoxyphenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one

After cooling to room temperature, ethyl acetate and hexane were added, and the resultant solid was collected and purified by recrystallization from ethyl acetate (59%), mp 196-197°C.

Analysis calculated for $C_{16}H_{16}N_4O_2$ 0.5 H_2O: C, 59.44; H, 5.88; N, 17.34.

Found: C, 59.37; H, 5.23; N, 17.12.

EXAMPLE 52

2-[4-(2-Diethylaminoethoxy)-phenylamino]-8-ethyl-8H-pyrido[2,3-d]-pyrimidin-7-one

After cooling to room temperature, the reaction mixture was partitioned between ethyl acetate and saturated sodium bicarbonate. The organic layer was washed with brine, dried over magnesium sulfate, filtered, and concentrated in vacuo. Hexane and ethyl acetate were added and the resultant solid removed by filtration. The solid was purified by flash chromatography eluting with a gradient of ethyl acetate to 5% methanol in ethyl acetate to 30% methanol in ethyl acetate (30%), mp 128-129°C.

Analysis calculated for $C_{21}H_{27}N_5O_2$ 0.5 H_2O: C, 64.62; H, 7.18; N, 17.95.

Found: C, 65.00; H, 7.11; N, 17.95.

EXAMPLE 53

8-Ethyl-2-[4-(4-methylpiperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]-pyrimidin-7-one

After cooling to room temperature, the reaction mixture was dissolved in chloroform and purified by flash chromatographed eluting with 30% methanol in ethyl acetate. The fractions containing product were concentrated and upon the addition of hexane and ethyl acetate, a solid was obtained and collected by filtration (26%), mp 185-186°C.

Analysis calculated for $C_{20}H_{24}N_6O$ 1.0 H_2O: C, 62.83; H, 6.81; N, 21.99.

Found: C, 63.12; H, 6.61; N, 21.78.

EXAMPLE 54

8-Ethyl-2-[3-(1,1,2,2-tetrafluoroethoxy)-phenylamino]-8H-pyrido[2,3-d]-pyrimidin-7-one

After cooling to room temperature, the reaction mixture was partitioned between ethyl acetate and saturated sodium bicarbonate. The organic layer was washed with brine, dried over magnesium sulfate, filtered, and concentrated in vacuo. The resultant solid was purified by flash chromatography eluting with ethyl acetate (20%), mp 175-176°C.

Analysis calculated for $C_{17}H_{14}N_4F_4O_2$: C, 53.41; H, 3.69; N, 14.65.

Found: C, 53.19; H, 3.81; N, 14.39.

EXAMPLE 55

8-Ethyl-2-(4-hydroxyphenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one

A mixture of 8-ethyl-2-(4-methoxyphenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one (133 mg, 0.45 mmol) and 1 mL of 48% aqueous HBr in 10 mL of propionic acid was heated at reflux for 3 hours. After cooling to room temperature, the reaction mixture was partitioned between ethyl acetate and saturated sodium bicarbonate. The aqueous layer was further extracted with ethyl acetate and the organic layers were combined and washed with brine, dried over magnesium sulfate, filtered, and concentrated in vacuo. The resultant solid was purified by dissolving in ethyl acetate and passing the solution through silica gel to provide 58 mg (46%) of 8-ethyl-2-(4 hydroxyphenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one, mp 222-224°C.

Analysis calculated for $C_{15}H_{14}N_4O_2$ 0.25 H_2O: C, 62.83; H, 5.06; N, 19.55.

Found: C, 63.12; H, 4.93; N, 19.18.

EXAMPLE 56

2-Benzyloxyphenylamino-8-ethyl-8H-pyrido[2,3-d]pyrimidin-7-one

A mixture of 8-ethyl-2-(4-hydroxyphenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one (94 mg, 0.33 mmol), benzyl bromide (70 mg, 0.41 mmol) and potassium carbonate (370 mg, 2.67 mmol) in 5 mL of dimethylformamide was heated at reflux for 5 minutes. After cooling to room temperature, water was added, and the resultant solid was collected and purified

by flash chromatography eluting with a gradient of 1:1 hexane:ethyl acetate to all ethyl acetate to provide 70 mg (56%) of 2-benzyloxyphenylamino-8-ethyl-8H-pyrido[2,3-d]pyrimidin-7-one, mp 195-197°C.

Analysis calculated for $C_{22}H_{20}N_4O_2$: C, 70.95; H, 5.41; N, 15.04.

Found: C, 70.56; H, 5.44; N, 14.86.

EXAMPLE 57

8-Ethyl-2-[4-(2-methoxyethoxy)phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one

A mixture of 8-ethyl-2-(4-hydroxyphenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one (92 mg, 0.33 mmol), 2-methoxyethyl bromide (55 mg, 0.40 mmol) and potassium carbonate (360 mg, 2.61 mmol) in 5 mL of dimethylformamide was heated at reflux for 5 minutes. After cooling to room temperature, water was added, and the resultant solid collected by filtration. The solid was dissolved in ethyl acetate and the solution dried over magnesium sulfate, filtered, concentrated, and purified by flash chromatography eluting with ethyl acetate to provide 92 mg (56%) of 8-ethyl-2-[4-(2-methoxyethoxy)phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one, mp 169-171°C.

Analysis calculated for $C_{18}H_{20}N_4O_3$ 0.25 H_2O: C, 62.70; H, 5.95; N, 16.26.

Found: C, 62.86; H, 5.87; N, 16.36.

EXAMPLE 58

8-(4-Methoxybenzyl)-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one

To a room temperature solution of 8-(4-methoxybenzylamino)-2-methanesulfanyl-8H-pyrido[2,3-d]pyrimidin-7-one (380 mg, 1.21 mmol) in 20 mL of chloroform was added *m*-CPBA (900 mg of 50%-60% *m*-CPBA, remainder water). The reaction was stirred at room temperature for 2 hours then partitioned between chloroform and saturated sodium bicarbonate. The organic layer was washed with additional saturated sodium bicarbonate followed by brine, dried over magnesium sulfate, filtered, and concentrated in vacuo. Upon the addition of chloroform and hexane, a solid formed and was collected to give 335 mg (62%) of 8-(4-methoxybenzylamino)-2-methanesulfonyl-8H-pyrido[2,3-d]pyrimidin-7-one.

A solution of 8-(4-methoxybenzylamino)-2-methanesulfonyl-8H-pyrido[2,3-d]pyrimidin-7-one (217 mg, 0.63 mmol) in 1.5 mL of aniline was heated at reflux for 10 minutes. Upon cooling to room temperature, a solid formed. Water (10 mL) was added, and the filtrate was decanted from the gummy solid that was then dissolved in ethyl acetate and purified by flash chromatography eluting with a gradient of 2:1 hexane:ethyl acetate to all ethyl acetate. The fractions containing product were concentrated in vacuo and treated with hexane and ethyl acetate. The solid was collected by filtration to provide 101 mg (45%) of 8-(4-methoxybenzyl)-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one, mp 215-216°C.

Analysis calculated for $C_{21}H_{18}N_4O_2$: C, 70.38; H, 5.06; N, 15.63.

Found: C, 70.06; H, 4.91; N, 15.47.

EXAMPLE 59

2-[4-(2-Diethylaminoethoxy)-phenylamino]-8-isopropyl-8H-pyrido[2,3-d]-pyrimidin-7-one

To 8-isopropyl-2-methanesulfinyl-8H-pyrido[2,3-d]pyrimidin-7-one (126 mg, 0.50 mmol) was added 4-(2-diethylaminoethoxy)aniline (313 mg, 1.51 mmol). The reaction mixture was heated at 175°C for 10 minutes then cooled to room temperature and partitioned between saturated sodium bicarbonate and ethyl acetate. The organic layer was dried over magnesium sulfate, filtered, and concentrated in vacuo. The residue was purified by flash chromatography eluting with 10% methanol in ethyl acetate. The fractions containing product were concentrated, and hexane was added. The resultant solid was collected by filtration to give 94 mg (47%) of 2-[4-(2-diethylaminoethoxy)-phenylamino]-8-isopropyl-8H-pyrido[2,3-d]pyrimidin-7-one, mp 84-85°C.

Analysis calculated for $C_{22}H_{29}N_5O_2$: C, 66.81; H, 7.39; N, 17.71.

Found: C, 66.63; H, 7.47; N, 17.72.

EXAMPLE 60

8-Isopropyl-2-[4-(4-methylpiperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]-pyrimidin-7-one

To 8-isopropyl-2-methanesulfinyl-8H-pyrido[2,3-d]pyrimidin-7-one (212 mg, 0.85 mmol) was added 4-(4-methylpiperazin-1-yl)-aniline (323 mg, 1.69 mmol). The reaction mixture was heated at 175°C for 10 minutes then cooled to room temperature and partitioned between saturated sodium bicarbonate and chloroform. The organic layer was washed with brine, dried over magnesium sulfate, filtered, and concentrated in vacuo. The residue was purified by flash chromatography eluting with 10% methanol in ethyl acetate. The fractions containing product were concentrated, and hexane and ethyl acetate were added to give a solid that was dissolved in chloroform and passed through an aluminum oxide column. The fractions containing product were concentrated, and upon addition of hexane and ethyl acetate, a solid formed providing 160 mg (50%) of 8-isopropyl-2-[4-(4-methylpiperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one, mp 221-222°C.

Analysis calculated for $C_{21}H_{26}N_6O$ 0.25 H_2O: C, 65.88; H, 6.93; N, 21.96.

Found: C, 66.18; H, 6.95; N, 21.57.

EXAMPLE 61

8-Methyl-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one

A mixture of 8-methyl-2-methanesulfonyl-8H-pyrido[2,3-d]pyrimidin-7-one (287 mg, 1.20 mmol) in 1 mL of aniline was heated at reflux for 10 minutes. The reaction mixture was partitioned between ethyl acetate and saturated sodium bicarbonate. The organic layer was washed with brine, dried over magnesium sulfate, and concentrated in vacuo. Upon addition of ethyl acetate and hexane, a precipitate formed and was collected to give 107 mg (35%) of product. An analytical sample of 8-methyl-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one was obtained by recrystallization from hexane and ethyl acetate followed by flash chromatography eluting with ethyl acetate, mp 244-247°C.

Analysis calculated for $C_{14}H_{12}N_4O$ 0.20 H_2O: C, 65.71; H, 4.88; N, 21.89.

Found: C, 65.73; H, 4.45; N, 21.55.

EXAMPLE 62

2-Amino-8-methyl-8H-pyrido[2,3-d]pyrimidin-7-one

8-Methyl-2-methanesulfanyl-8H-pyrido[2,3-d]pyrimidin-7-one (160 mg, 0.77 mmol) was dissolved in 15 mL of methanolic ammonia and heated in a sealed glass tube at 120°C for 35 hours. The resultant crystals were collected by filtration washing with 1:1 hexane:ethyl acetate to give 77 mg (57%) of 2-amino-8-methyl-8H-pyrido[2,3-d]pyrimidin-7-one, mp 237-253°C.

Analysis calculated for $C_8H_8N_4O$ 0.15 H_2O: C, 53.71; H, 4.68; N, 31.32.

Found: C, 53.86; H, 4.69; N, 31.00.

EXAMPLE 63

2-Benzylamino-8-methyl-8H-pyrido[2,3-d]pyrimidin-7-one

A solution of 8-methyl-2-methanesulfanyl-8H-pyrido[2,3-d]pyrimidin-7-one (171 mg, 0.83 mmol) in 1.5 mL of benzylamine was heated at reflux for 3 hours. The solid that formed upon cooling was collected by filtration, washed with 1:1 hexane:ethyl acetate, and then chromatographed eluting with ethyl acetate to give 95 mg (43%) of 2-benzylamino-8-methyl-8H-pyrido[2,3-d]pyrimidin-7-one, mp 160-162°C.

Analysis calculated for $C_{15}H_{14}N_4O$: C, 67.65; H, 5.30; N, 21.04.

Found: C, 67.81; H, 5.07; N, 20.99.

EXAMPLE 64

2-Butylamino-8-methyl-8H-pyrido[2,3-d]pyrimidin-7-one

A solution of 8-methyl-2-methanesulfonyl-8H-pyrido[2,3-d]pyrimidin-7-one (200 mg, 0.83 mmol) in 2 mL of n-butylamine was stirred at room temperature for 10 minutes. The reaction mixture was partitioned between ethyl acetate and water, and the organic layer was washed with saturated sodium bicarbonate and brine, dried over magnesium sulfate, and concentrated in vacuo. A 4:1 mixture of hexane:ethyl acetate was added to the residue and the resultant

solid collected by filtration to give 154 mg (79%) of 2-butylamino-8-methyl-8H-pyrido[2,3-d]pyrimidin-7-one, mp 146-147°C.

Analysis calculated for $C_{12}H_{16}N_4O$: C, 62.05; H, 6.94; N, 24.12.

Found: C, 61.91; H, 6.86; N, 24.13.

EXAMPLE 65

2-Ethylamino-8-methyl-8H-pyrido[2,3-d]pyrimidin-7-one

A mixture of 8-methyl-2-methanesulfonyl-8H-pyrido[2,3-d]pyrimidin-7-one (152 mg, 0.63 mmol) in 2.5 mL of 70% aqueous ethylamine was stirred at room temperature for 10 minutes. The reaction mixture was partitioned between ethyl acetate and water, and the organic layer was washed with saturated sodium bicarbonate and brine, dried over magnesium sulfate, and concentrated in vacuo to give 105 mg (82%) of 2-ethylamino 8-methyl-8H-pyrido[2,3-d]pyrimidin-7-one, mp 194-195°C.

Analysis calculated for $C_{10}H_{12}N_4O$: C, 58.81; H, 5.92; N, 27.43.

Found: C, 58.44; H, 5.80; N, 27.15.

EXAMPLE 66

8-Methyl-2-(2-pyridin-2-yl-ethylamino)-8H-pyrido[2,3-d]pyrimidin-7-one

A mixture of 8-methyl-2-methanesulfonyl-8H-pyrido[2,3-d]pyrimidin-7-one (165 mg, 0.69 mmol) and 2-(2-aminoethyl)-pyridine (165 μL, 1.38 mmol) in 2 mL of tetrahydrofuran was stirred at room temperature for 30 minutes. The solid was collected to give 40 mg (21%) of product. The filtrate was concentrated and purified by flash chromatography to give 125 mg (64%) of 8-methyl-2-(2-pyridin-2-yl-ethylamino)-8H-pyrido[2,3-d]pyrimidin-7-one, mp 155-156°C.

Analysis calculated for $C_{15}H_{15}N_5O$ 0.20 H_2O: C, 63.03; H, 5.46; N, 24.51.

Found: C, 63.31; H, 5.18; N, 24.75.

EXAMPLE 67

2-Isopropylamino-8-methyl-8H-pyrido[2,3-d]pyrimidin-7-one

A mixture of 8-methyl-2-methanesulfonyl-8H-pyrido[2,3-d]pyrimidin-7-one (194 mg, 0.81 mmol) and 2 mL of isopropylamine was stirred at room temperature for 15 minutes. Excess amine was removed in vacuo, and the residue

was partitioned between ethyl acetate and water. The organic phase was washed with saturated sodium bicarbonate, followed by brine, dried over magnesium sulfate, and concentrated to give 168 mg (95%) of 2-isopropylamino-8-methyl-8H-pyrido[2,3-d]pyrimidin-7-one, mp 148-149°C.

Analysis calculated for $C_{11}H_{14}N_4O$: C, 60.53; H, 6.47; N, 25.67.

Found: C, 60.27; H, 6.50; N, 25.60.

EXAMPLE 68

3-(4-Ethylamino-2-phenylamino-pyrimidin-5-yl)propionic acid ethyl ester

A mixture of ethyl 3-(4-ethylamino-2-phenylamino-pyrimidin-5-yl)acrylate (152 mg, 0.48 mmol) and 5% palladium on carbon in a solvent mixture of ethanol and tetrahydrofuran was hydrogenated under pressure. The catalyst was filtered off and the filtrate concentrated. The residue was purified by flash chromatography eluting with 2:1 ethyl acetate:hexane to give 72 mg (47%) of 3-(4-ethylamino-2-phenylamino-pyrimidin-5-yl)propionic acid ethyl ester, mp 106-107°C.

Analysis calculated for $C_{17}H_{22}N_4O_2$: C, 64.95; H, 7.05; N, 17.82.

Found: C, 64.90; H, 7.06; N, 17.77.

EXAMPLE 69

8-Ethyl-2-phenylamino-5,8-dihydro-6H-pyrido[2,3-d]pyrimidin-7-one

A mixture of 3-(4-ethylamino-2-phenylamino-pyrimidin-5-yl)propionic acid ethyl ester (254 mg, 0.81 mmol) and 141 mg (0.93 mmol) of 1,8-diazabicyclo[5.4.0]undec-7-ene in 5 mL of N,N-diisopropylethylamine was heated at reflux overnight. Additional 1,8-diazabicyclo[5.4.0]undec-7-ene (121 μL, 1.0 mmol) was added, and the reaction was heated at reflux for 24 hours. Upon cooling to room temperature, a solid formed that was collected by filtration and purified by flash chromatography eluting with ethyl acetate to give 110 mg (51%) of 3-(4-ethylamino-2-phenylamino-pyrimidin-5-yl)propionic acid ethyl ester, mp 146-147°C.

Analysis calculated for $C_{15}H_{16}N_4O$: C, 67.15; H, 6.01; N, 20.88.

Found: C, 67.06; H, 6.06; N, 20.59.

EXAMPLE 70

3-(4-Methylamino-2-methanesulfanyl-pyrimidin-5-yl)-acrylonitrile

To a room temperature suspension of sodium hydride (240 mg of a 60% suspension of NaH in oil) in 10 mL of dimethylformamide was added diethyl cyanomethylphosphonate (1.0 mL, 6.17 mmol). The reaction mixture was stirred at room temperature for 15 minutes, then 4-methylamino-2-methanesulfanyl-pyrimidine-5-carbaldeyde (1.02 g, 5.57 mmol) in 10 mL of dimethylformamide was added, and the mixture was stirred at room temperature for 10 minutes. The reaction mixture was partitioned between brine and a 1:1 mixture of hexane and ethyl acetate. The organic layer was washed with water, dried over magnesium sulfate, and concentrated to provide 367 mg (32%) of 3-(4-methylamino-2-methanesulfanyl-pyrimidin-5-yl)acrylonitrile, mp 207-210°C. The residue was purified by flash chromatography eluting with 1:1 ethyl acetate:hexane to provide an additional 19 mg (13%) of product.

Analysis calculated for $C_9H_{10}N_4S$ 0.5 H_2O: C, 50.20; H, 5.15; N, 26.02.

Found: C, 50.48; H, 4.80; N, 26.28.

EXAMPLE 71

8-Methyl-2-methanesulfanyl-8H-pyrido[2,3-d]pyrimidin-7-ylideneamine

A mixture of 3-(4-methylamino-2-methanesulfanyl-pyrimidin-5-yl)acrylonitrile (805 mg, 3.91 mmol) and 3 mL (20.13 mmol) of 1,8-diazabicyclo[5.4.0]undec-7-ene in 15 mL of N,N-diisopropylethylamine was heated at reflux overnight. The liquid was decanted from the black oil and purified by flash chromatography eluting with a mixture of 1:3 methanol:ethyl acetate. The fractions containing product were concentrated and a 1:4 mixture of ethyl acetate:hexane was added to the residue. The resultant solid was collected by filtration to give 133 mg (16%) of 8-methyl-2-methanesulfanyl-8H-pyrido[2,3-d]pyrimidin-7-ylideneamine, mp 146-149°C. Concentration of the filtrate provided an additional 405 mg (56%) of product.

Analysis calculated for $C_9H_{10}N_4S$ 0.65 H_2O: C, 49.59; H, 5.23; N, 25.70.

Found: C, 49.26; H, 4.83; N, 25.48.

EXAMPLE 72

3-(4-Ethylamino-2-phenylamino-pyrimidin-5-yl)acrylonitrile

To a room temperature suspension of sodium hydride (38 mg of a 60% suspension of NaH in oil) in 5 mL of dimethylformamide was added diethyl cyanomethylphosphonate (150 μL, 0.93 mmol). The reaction mixture was stirred at room temperature for 15 minutes, then 4-ethylamino-2-phenylamino-pyrimidine-5-carbaldeyde (200 mg, 0.83 mmol) in 2 mL of dimethylformamide was added, and the mixture was stirred at room temperature for 10 minutes. The reaction mixture was partitioned between brine and ethyl acetate. The organic layer was washed with water, dried over magnesium sulfate, and concentrated in vacuo The residue was purified by flash chromatography eluting with 1:1 ethyl acetate:hexane. The fractions containing product were concentrated, and hexane was added to the residue. The resultant solid was collected by filtration to give 91 mg (43%) of 3-(4-ethylamino-2-phenylamino-pyrimidin-5-yl)acrylonitrile, mp 244-246°C. Concentration of the filtrate provided an additional 68 mg (32%) of product.

Analysis calculated for $C_{15}H_{15}N_5$: C, 67.91; H, 5.70; N, 26.40.

Found: C, 67.80; H, 5.57; N, 26.39.

EXAMPLE 73

3-(4-Ethylamino-2-phenylamino-pyrimidin-5-yl)-but-2-enoic acid ethyl ester

To a room temperature solution of 4-ethylamino-2-phenylamino-pyrimidine-5-carboxaldehyde (200 mg, 0.83 mmol) in 10 mL of tetrahydrofuran was added (carbethoxyethylidene)triphenylphosphorane (360 mg, 1.0 mmol). The reaction mixture was heated at reflux overnight, cooled, and concentrated in vacuo. The residue was purified by flash chromatography eluting with 1:1 ethyl acetate:hexane. The fractions containing product were concentrated, and 1:2 ethyl acetate:hexane was added to the residue. The resultant solid was collected by filtration to provide 176 mg (65%) of 3-(4-ethylamino-2-phenylamino-pyrimidin-5-yl)-but-2-enoic acid ethyl ester, mp 148-150°C.

Analysis calculated for $C_{18}H_{22}N_4O_2$: C, 66.24; H, 6.79; N, 17.16.

Found: C, 65.95; H, 6.68; N, 17.02.

EXAMPLE 74

8-(1-Ethylpropyl)-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one

To a suspension of NaH (33 mg of a 60% suspension of NaH in mineral oil) in 7 mL of dimethylformamide was added 2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one (154 mg, 0.65 mmol). The reaction mixture was heated to 60°C resulting in a clear solution. The solution was cooled slightly, and 3-bromopentane (125 μL, 1.01 mmol) was added. The reaction was heated at 60°C for 30 minutes, then cooled to room temperature and partitioned between water and ethyl acetate. The organic layer was dried over magnesium sulfate, filtered, and concentrated in vacuo. The residue was purified by flash chromatography eluting with 1:1 ethyl acetate:hexane to provide 45 mg (23%) of 8-(1-ethylpropyl)-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one, mp 116-118°C.

Analysis calculated for $C_{18}H_{20}46O$ 0.2 H_2O: C, 69.29; H, 6.59; N, 17.95.
Found: C, 69.59; H, 6.41; N, 18.03.

EXAMPLE 75

8-Isopentyl-2-methanesulfanyl-8H-pyrido[2,3-d]pyrimidin-7-one

To a suspension of NaH (150 mg of a 60% suspension of NaH in mineral oil) in 10 mL of dimethylformamide was added 2-methanesulfanyl-8H-pyrido[2,3-d]pyrimidin-7-one (508 mg, 2.63 mmol). The reaction mixture was heated to 50°C resulting in an orange solution. The solution was cooled slightly, and 3-bromopentane (500 μL, 3.97 mmol) was added. The reaction was heated at 50°C for 1 hour, then cooled to room temperature and partitioned between water and ethyl acetate. The organic layer was dried over magnesium sulfate, filtered, and concentrated in vacuo. The residue was purified by flash chromatography eluting with a gradient of 1:3 ethyl acetate:hexane to all ethyl acetate to provide 348 mg (50%) of 8-isopentyl-2-methanesulfanyl-8H-pyrido[2,3-d]pyrimidin-7-one, as an oil.

EXAMPLE 76

8-(1-Ethylpropyl)-2-methanesulfinyl-8H-pyrido[2,3-d]pyrimidin-7-one

To a room temperature solution of 8-(1-ethylpropyl)-2-methanesulfanyl-8H-pyrido[2,3-d]pyrimidin-7-one (260 mg, 0.99 mmol) in 10 mL of chloroform was added (±)-*trans*-2-(phenylsulfonyl)-3-phenyloxaziridine (260 mg, 1.11 mmol). The solution was stirred at room temperature overnight then concentrated in vacuo. The residue was purified by flash chromatography eluting with a gradient of ethyl acetate to 10% methanol in ethyl acetate to provide 227 mg (82%) of 8-(1-ethylpropyl)-2-methanesulfinyl-8H-pyrido[2,3-d]pyrimidin-7-one, mp 111-114°C.

Analysis calculated for $C_{13}H_{17}N_3O_2S$: C, 55.89; H, 6.13; N, 15.04.

Found: C, 55.70; H, 6.02; N, 14.95.

EXAMPLE 77

8-(1-Ethylpropyl)-2-[4-(4-methylpiperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one

To 8-(1-ethylpropyl)-2-methanesulfinyl-8H-pyrido[2,3-d]pyrimidin-7-one (190 mg, 0.68 mmol) was added 4-(4-methylpiperazin-1-yl)-aniline (260 mg, 1.36 mmol). The reaction mixture was heated at 175°C for 10 minutes, then cooled to room temperature and partitioned between saturated sodium bicarbonate and chloroform. The organic layer was washed with saturated sodium bicarbonate and brine, dried over magnesium sulfate, filtered, and concentrated in vacuo. The residue was purified by flash chromatography eluting with 10% methanol in ethyl acetate. The fractions containing product were concentrated, the solid was dissolved in chloroform, and a large amount of hexane was added. The solution was cooled in the refrigerator overnight, and the resultant precipitate was collected by filtration to give 101 mg (37%) of product. An analytical sample was obtained by recrystallization from chloroform and hexane to give 41 mg of 8-(1-ethylpropyl)-2-[4-(4-methylpiperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one, mp 155-157°C.

Analysis calculated for $C_{23}H_{30}N_6O$ 0.10 H_2O: C, 67.68; H, 7.41; N, 20.60.

Found: C, 67.31; H, 7.25; N, 20.40.

EXAMPLE 78

2-(4-Diethylamino-phenylamino)-8-ethyl-8H-pyrido[2,3-d]pyrimidin-7-one

A mixture of 8-ethyl-2-methanesulfinyl-8H-pyrido[2,3-d]pyrimidin-7-one (129 mg, 0.54 mmol) and 1 mL of 4-diethylaminoaniline was heated at 175°C for 10 minutes, then cooled to room temperature and partitioned between saturated sodium bicarbonate and ethyl acetate. The organic layer was washed with saturated sodium bicarbonate and brine, dried over magnesium sulfate, filtered, and concentrated in vacuo. The residue was purified by flash chromatography eluting with ethyl acetate. The fractions containing product were concentrated, and hexane was added to the residue. The resultant precipitate was collected by filtration to give 124 mg (68%) of 2-(4-diethylamino-phenylamino)-8-ethyl-8H-pyrido[2,3-d]pyrimidin-7-one, mp 108-109°C.

Analysis calculated for $C_{19}H_{23}N_5O$: C, 67.63; H, 6.87; N, 20.76.

Found: C, 67.49; H, 6.79; N, 20.78.

EXAMPLE 79

8-Ethyl-2-(4-morpholin-4-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one

A mixture of 8-ethyl-2-methanesulfinyl-8H-pyrido[2,3-d]pyrimidin-7-one (136 mg, 0.57 mmol) and 4-morpholinoaniline (205 mg, 1.15 mmol) was heated at 175°C for 10 minutes then cooled to room temperature, and ethyl acetate was added. The precipitate was collected by filtration and purified by flash chromatography eluting with ethyl acetate. The fractions containing product were concentrated, and ethyl acetate and hexane were added to the residue. The resultant precipitate was collected by filtration to give 114 mg (57%) yield of 8-ethyl-2-(4-morpholin-4-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one, mp 227-228°C.

Analysis calculated for $C_{19}H_{21}N_5O_2$ 0.25 H_2O: C, 64.14; H, 6.05; N, 19.69.

Found: C, 64.37; H, 5.80; N, 19.78.

EXAMPLE 80

6-Methyl-2-methylsulfanyl-8H-pyrido[2,3-d]pyrimidin-7-one

A solution of methyl 2-[bis(2,2,2-trifluoroethoxy)phosphinyl]propionate (*Tetrahedron Lett.*, 1983:4405) (526 mg, 1.59 mmol) and 18-crown-6 (1.611 g,

6.10 mmol) in 15 mL of tetrahydrofuran was cooled to -78°C and potassium bis(trimethylsilyl)amide (3.17 mL of a 0.5 M solution in toluene) was added followed by 4-amino-2-methanesulfanyl-pyrimidine-5-carboxaldehyde (206 mg, 1.22 mmol). The reaction mixture was stirred at -78°C for 30 minutes then allowed to warm to room temperature. After stirring at room temperature for 2.5 hours, the reaction was quenched with saturated ammonium chloride. The aqueous layer was extracted with ether several times, and the combined extracts were dried over magnesium sulfate, filtered, and concentrated. Hexane and ethyl acetate were added to the residue, and the resultant solid was collected to provide122 mg (48%) of 6-methyl-2-methylsulfanyl 8H-pyrido[2,3-d]pyrimidin-7-one, mp 243-245°C.

Analysis calculated for $C_9H_9N_3OS$ 0.10 H_2O: C, 51.72; H, 4.41; N, 20.11. Found: C, 51.42; H, 4.36; N, 19.96.

EXAMPLE 81

8-Ethyl-6-methyl-2-methylsulfanyl-8H-pyrido[2,3-d]pyrimidin-7-one

To a suspension of NaH (261 mg of a 60% suspension of NaH in mineral oil) in 40 mL of dimethylformamide was added 6-methyl-2-methylsulfanyl-8H-pyrido[2,3-d]pyrimidin-7-one (926 mg, 4.48 mmol). The reaction mixture was heated to 50°C resulting in a clear solution. The solution was cooled slightly, and iodoethane (491 μL, 6.14 mmol) was added. The reaction was heated at 50°C for 10 minutes, then cooled to room temperature and partitioned between ice water and ethyl acetate. The organic layer was dried over magnesium sulfate, filtered, and concentrated in vacuo. The residue was partitioned between hexane and water. The organic layer was dried over magnesium sulfate, filtered, and concentrated in vacuo. Hexane was added and the resultant solid collected by filtration to provide 824 mg (78%) of 8-ethyl-6-methyl-2-methylsulfanyl-8H-pyrido[2,3-d]pyrimidin-7-one, mp 84-86°C.

Analysis calculated for $C_{11}H_{13}N_3OS$ 0.05 H_2O 0.05 ethyl acetate: C, 55.93; H, 5.62; N, 17.48. Found: C, 56.11; H, 5.62; N, 17.21.

EXAMPLE 82

8-Ethyl-2-methanesulfinyl-6-methyl-8H-pyrido[2,3-d]pyrimidin-7-one

To a room temperature solution of 8-ethyl-6-methyl-2-methylsulfanyl-8H-pyrido[2,3-d]pyrimidin-7-one (789 mg, 3.36 mmol) in 50 mL of chloroform was added (±)-*trans*-2-(phenylsulfonyl)-3-phenyloxaziridine (1.06 g, 4.06 mmol). The solution was stirred at room temperature overnight then concentrated in vacuo. The residue was purified by flash chromatography eluting with a gradient of ethyl acetate to 10% methanol in ethyl acetate to provide 743 mg (88%) of 8-ethyl-6-methyl-2-methylsulfinyl-8H-pyrido[2,3-d]pyrimidin-7-one, mp 148-150°C. Analysis calculated for $C_{11}H_{13}N_3O_2S$ 0.20 H_2O: C, 51.85; H, 5.26; N, 16.49. Found: C, 52.22; H, 5.14; N, 16.09.

EXAMPLE 83

8-Ethyl-6-methyl-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one

A mixture of 8-ethyl-6-methyl-2-methylsulfinyl-8H-pyrido[2,3-d]pyrimidin-7-one (123 mg, 0.49 mmol) and 1 mL of aniline was heated at 175°C for 20 minutes. The reaction was cooled to room temperature and partitioned between ethyl acetate and saturated sodium bicarbonate. The organic layer was washed with brine, dried over magnesium sulfate, filtered, and concentrated. Hexane was added to the residue, and the resultant solid was collected by filtration and purified by flash chromatography eluting with ethyl acetate to provide 21 mg (15%) of 8-ethyl-6-methyl-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one, mp 178-180°C.
Analysis calculated for $C_{16}H_{16}N_4O$ 0.10 H_2O 0.05 ethyl acetate: C, 67.92; H, 5.80; N, 19.57. Found: C, 67.64; H, 5.50; N, 19.18.

EXAMPLE 84

8-Ethyl-6-methyl-2-[4-(4-methyl-piperazin-1-yl)-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one

A mixture of 8-ethyl-6-methyl-2-methylsulfinyl-8H-pyrido[2,3-d]pyrimidin-7-one (154 mg, 0.61 mmol) and 234 mg (1.23 mmol) of 4-(4-methyl-piperazin-1-yl)-aniline was heated at 175°C for 30 minutes. The

reaction was cooled to 100°C, and water was added. The water was decanted off, and the gum was dissolved in chloroform and washed with saturated sodium bicarbonate followed by brine. The organic layer was dried over magnesium sulfate, filtered, and concentrated. The residue was purified by flash chromatography eluting with 10% methanol in chloroform. The fractions containing product were collected and concentrated. The residue was recrystallized from hexane and ethyl acetate and then recrystallized again from chloroform and hexane to provide 76 mg (33%) of 8-ethyl-6-methyl-2-[4-(4-methyl-piperazin-1-yl)-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one, mp 198-200°C.

Analysis calculated for $C_{21}H_{26}N_6O$ 0.3 H_2O: C, 65.73; H, 6.94; N, 21.91.

Found: C, 65.35; H, 6.66; N, 21.84.

EXAMPLE 85

8-sec-Butyl-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one

To a suspension of NaH (47 mg of a 60% suspension of NaH in mineral oil) in 6 mL of dimethylformamide was added 2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one (202 mg, 0.85 mmol). The reaction mixture was heated to 50°C to 60°C resulting in a yellow solution. The solution was cooled slightly, and 2-iodobutane (140 μL, 1.22 mmol) was added. The reaction was heated at 50°C for 20 minutes, then cooled to room temperature and partitioned between water and ethyl acetate. The organic layer was dried over magnesium sulfate, filtered, and concentrated in vacuo. Purification by flash chromatography eluting with 2:1 ethyl acetate:hexane gave 29 mg (12%) of 8-sec-butyl-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one, mp 155-156°C.

Analysis calculated for $C_{17}H_{18}N_4O$: C, 69.37; H, 6.16; N, 19.03.

Found: C, 69.18; H, 5.92; N, 18.91.

EXAMPLE 86

8-(2-Methoxyethyl)-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one

To a suspension of NaH (49 mg of a 60% suspension of NaH in mineral oil) in 6 mL of dimethylformamide was added 2-phenylamino-8H-

pyrido[2,3-d]pyrimidin-7-one (200 mg, 0.84 mmol). The reaction mixture was heated to 50°C resulting in a yellow solution. The solution was cooled slightly, and 2-bromoethylmethyl ether (140 μL, 1.49 mmol) was added. The reaction mixture was heated at 50°C for 10 minutes, then cooled to room temperature and partitioned between water and ethyl acetate. The organic layer was dried over magnesium sulfate, filtered, and concentrated in vacuo. Purification by flash chromatography eluting with a gradient of 2:1 hexane:ethyl acetate to all ethyl acetate gave 140 mg (56%) of 8-(2-methoxyethyl)-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one, mp 179-180°C.

Analysis calculated for $C_{16}H_{16}N_4O_2$ 0.2 H_2O: C, 64.07; H, 5.51; N, 18.68.
Found: C, 64.02; H, 5.36; N, 18.51.

EXAMPLE 87

8-(3-Phenoxypropyl)-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one

To a suspension of NaH (51 mg of a 60% suspension of NaH in mineral oil) in 6 mL of dimethylformamide was added 2-phenylamino-8H-pyrido[2,3-d]-pyrimidin-7-one (200 mg, 0.84 mmol). The reaction mixture was heated to 50°C resulting in a yellow solution. The solution was cooled slightly, and 3-phenoxypropyl bromide (230 μL, 1.47 mmol) was added. The reaction mixture was heated at 50°C for 10 minutes, then cooled to room temperature and partitioned between water and ethyl acetate. The organic layer was dried over magnesium sulfate, filtered, and concentrated in vacuo. Methanol and ethyl acetate were added to the residue, and 60 mg (19%) of 8-(3-phenoxypropyl)-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one was collected by filtration, mp 175-176°C.

Analysis calculated for $C_{22}H_{20}N_4O_2$: C, 70.95; H, 5.41; N, 15.04.
Found: C, 70.67; H, 5.42; N, 14.98.

EXAMPLE 88

8-Ethyl-2-(4-fluorophenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one

A mixture of 8-ethyl-2-methylsulfinyl-8H-pyrido[2,3-d]pyrimidin-7-one (145 mg, 0.61 mmol) and 500 μL of 4-fluoroaniline was heated at 175°C for

10 minutes. The reaction mixture was cooled to room temperature, and the resultant solid was washed with 1:1 hexane:ethyl acetate. The solid was purified by flash chromatography eluting with ethyl acetate to provide 85 mg (49%) of 8-ethyl-2-(4-fluorophenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one, mp 215-217°C.

Analysis calculated for $C_{15}H_{13}N_4OF$: C, 63.37; H, 4.61; N, 19.71.

Found: C, 62.98; H, 4.37; N, 19.60.

EXAMPLE 89

8-Ethyl-2-(3-fluorophenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one

A mixture of 8-ethyl-2-methylsulfinyl-8H-pyrido[2,3-d]pyrimidin-7-one (112 mg, 0.47 mmol) and 500 μL of 3-fluoroaniline was heated at 175°C for 10 minutes. The reaction mixture was cooled to room temperature and partitioned between ethyl acetate and saturated sodium bicarbonate. The organic layer was washed with brine, dried over magnesium sulfate, filtered, and concentrated in vacuo. The residue was purified by flash chromatography eluting with ethyl acetate. Recrystallization from chloroform and hexane provided 33 mg (25%) of 8-ethyl-2-(3-fluorophenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one, mp 210-212°C.

Analysis calculated for $C_{15}H_{13}N_4OF$ 0.1 H_2O 0.1 ethyl acetate: C, 62.73; H, 4.75; N, 19.01. Found: C, 62.70; H, 4.64; N, 18.80.

EXAMPLE 90

8-Ethyl-2-(3-fluoro-4-methoxyphenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one

A mixture of 8-ethyl-2-methylsulfinyl-8H-pyrido[2,3-d]pyrimidin-7-one (124 mg, 0.52 mmol) and 148 mg (1.05 mmol) of 3-fluoro-4-methoxyaniline was heated at 175°C for 10 minutes. The reaction mixture was cooled to room temperature and partitioned between ethyl acetate and saturated sodium bicarbonate. The organic layer was washed with brine, dried over magnesium sulfate, filtered, and concentrated in vacuo. The residue was purified by flash chromatography eluting with ethyl acetate. Recrystallization from ethyl acetate

and hexane provided 67 mg (41%) of 8-ethyl-2-(3-fluoro-4-methoxyphenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one, mp 196-198°C.
Analysis calculated for $C_{16}H_{15}N_4O_2F$ 0.3 H_2O: C, 60.11; H, 4.88; N, 17.53.
Found: C, 60.13; H, 4.78; N, 17.15.

EXAMPLE 91

8-Ethyl-2-(3-fluoro-2-methoxyphenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one

A mixture of 8-ethyl-2-methylsulfinyl-8H-pyrido[2,3-d]pyrimidin-7-one (133 mg, 0.56 mmol) and 500 μL of 3-fluoro-2-methoxyaniline was heated at 175°C for 20 minutes. The reaction mixture was cooled to room temperature and partitioned between ethyl acetate and saturated sodium bicarbonate. The organic layer was washed with brine, dried over magnesium sulfate, filtered, and concentrated in vacuo. The residue was purified by flash chromatography eluting with ethyl acetate. Recrystallization from ethyl acetate and hexane provided 28 mg (16%) of 8-ethyl 2-(3-fluoro-2-methoxyphenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one, mp 92-93°C.
Analysis calculated for $C_{16}H_{15}N_4O_2F$ 0.15 H_2O: C, 60.63; H, 4.83; N, 17.68.
Found: C, 60.31; H, 4.52; N, 17.42.

EXAMPLE 92

8-Ethyl-2-(2-methoxyphenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one

A mixture of 8-ethyl-2-methylsulfinyl-8H-pyrido[2,3-d]pyrimidin-7-one (140 mg, 0.59 mmol) and 500 μL of 2-methoxyaniline was heated at 175°C for 20 minutes. The reaction mixture was cooled to room temperature and partitioned between chloroform and saturated sodium bicarbonate. The organic layer was washed with brine, dried over magnesium sulfate, filtered, and concentrated in vacuo. The residue was purified by flash chromatography eluting with ethyl acetate. Recrystallization from ethyl acetate and hexane provided 60 mg (34%) of 8-ethyl-2-(2-methoxyphenyl-amino)-8H-pyrido[2,3-d]pyrimidin-7-one, mp 126-128°C.

Analysis calculated for $C_{16}H_{16}N_4O_2$ 0.2 H_2O: C, 64.09; H, 5.47; N, 18.69. Found: C, 64.10; H, 5.36; N, 18.44.

EXAMPLE 93

2-(4-Dimethylamino-phenylamino)-8-ethyl-8H-pyrido[2,3-d]pyrimidin-7-one

A mixture of 8-ethyl-2-methanesulfinyl-8H-pyrido[2,3-d]pyrimidin-7-one (155 mg, 0.65 mmol) and 500 μL of 4-dimethylaminoaniline was heated at 175°C for 10 minutes, then cooled to room temperature and partitioned between saturated sodium bicarbonate and ethyl acetate. The organic layer was washed with brine, dried over magnesium sulfate, filtered, and concentrated in vacuo. The resultant solid was washed with hexane and ethyl acetate then purified by flash chromatography eluting with ethyl acetate. The fractions containing product were concentrated and a 2:1 mixture of hexane and ethyl acetate was added to the residue. The resultant precipitate was collected by filtration to give 110 mg (50%) of 2-(4-dimethylamino-phenylamino)-8-ethyl-8H-pyrido[2,3-d]pyrimidin-7-one, mp 189-191°C.

Analysis calculated for $C_{17}H_{19}N_5O$ 0.2 H_2O 0.25 ethyl acetate: C, 64.55; H, 6.40; N, 20.92. Found: C, 64.55; H, 6.32; N, 21.10.

EXAMPLE 94

2-Methanesulfanyl-4-phenylamino-pyrimidine-5-carboxylic acid ethyl ester

To a room temperature solution of 4-chloro-2-methanesulfanyl-pyrimidine-5-carboxylic acid ethyl ester (9.25 g , 40.0 mmol) in 100 mL of tetrahydrofuran was added 16 mL of triethylamine followed by aniline (4.0 mL, 43.8 mmol). The solution was stirred at room temperature overnight. The white solid was removed by filtration washing with ethyl acetate. The filtrate was concentrated in vacuo and partitioned between chloroform and saturated aqueous sodium bicarbonate. The organic layer was dried over magnesium sulfate, filtered, and concentrated. A solution of 2:1 hexane:ethyl acetate was added to the residue, and the resultant white solid was collected to provide 7.07 g (60%) of product . An additional 2.18 g (18%) was obtained from the filtrate. Recrystallization from hexane and ethyl acetate provided an analytical sample of 2-methanesulfanyl-4-phenylamino-pyrimidine-5-carboxylic acid ethyl ester, mp 86-87.5°C.

Analysis calculated for $C_{14}H_{15}N_3O_2S$: C, 58.11; H, 5.23; N, 14.52.

Found: C, 57.93; H, 5.27; N, 14.46.

EXAMPLE 95

(2-Methanesulfanyl-4-phenylamino-pyrimidin-5-yl)-methanol

A solution of 2-methanesulfanyl-4-phenylamino-pyrimidine-5-carboxylic acid ethyl ester (7.25 g, 25.1 mmol) in 100 mL of tetrahydrofuran was added dropwise to a room temperature suspension of lithium aluminum hydride (1.55 g, 40.9 mmol) in 100 mL of tetrahydrofuran. After 10 minutes, an additional 1.00 g of lithium aluminum hydride was added to the reaction mixture, and stirring was continued for 1.5 hours. The reaction was carefully quenched with isopropanol followed by 6 mL of water, 10 mL of 15% NaOH, and 20 mL of water, and the mixture was stirred for 1.5 hours. The white precipitate was removed by filtration washing with ethyl acetate. The filtrate was washed with water, dried over magnesium sulfate, filtered, and concentrated in vacuo. Purification by flash chromatography eluting with ethyl acetate provided 2.22 g (36%) of (4-ethylamino-2-methanesulfanyl-pyrimidin-5-yl)-methanol, mp 127-128°C.

Analysis calculated for $C_{12}H_{13}N_3OS$: C, 58.28; H, 5.30; N, 16.99.

Found: C, 58.15; H, 5.09; N, 16.90.

EXAMPLE 96

2-Methanesulfanyl-4-phenylamino-pyrimidine-5-carboxaldehyde

To (4-ethylamino-2-methanesulfanyl-pyrimidin-5-yl)-methanol (2.80 g, 11.4 mmol) in 400 mL of chloroform was added manganese oxide (3.95 g, 45.4 mmol). The suspension was stirred at room temperature overnight. The mixture was filtered through celite washing with chloroform. The filtrate was concentrated in vacuo to give 2.73 g (98%) of 2-methanesulfanyl-4-phenylamino-pyrimidine-5-carboxaldehyde, mp 89-90°C.

Analysis calculated for $C_{12}H_{11}N_3OS$: C, 58.76; H, 4.52; N, 17.13.

Found: C, 58.56; H, 4.69; N, 17.10.

EXAMPLE 97

Ethyl 3-(2-Methanesulfanyl-4-phenylamino-pyrimidin-5-yl)acrylate

To a room temperature solution of 2-methanesulfanyl-4-phenylamino pyrimidine-5-carboxaldehyde (1.00 g, 4.08 mmol) in 20 mL of tetrahydrofuran was added (carbethoxymethylene)triphenylphosphorane (1.82 g, 5.22 mmol). The reaction mixture was heated at reflux for 70 minutes, then concentrated in vacuo and partitioned between ethyl acetate and 1N HCl. The organic layer was extracted with two additional portions of 1N HCl, and the acid layers were combined and neutralized with saturated sodium bicarbonate. The product was extracted into ethyl acetate, dried over magnesium sulfate, filtered, and concentrated in vacuo. The residue was purified by flash chromatography eluting with ethyl acetate to provide 988 mg (77%) of ethyl 3-(2-methanesulfanyl-4-phenylamino-pyrimidin-5-yl)acrylate as a yellow oil.

EXAMPLE 98

2-Methanesulfanyl-8-phenyl-8H-pyrido[2,3-d]pyrimidin-7-one

To a room temperature solution of ethyl 3-(2-methanesulfanyl-4-phenylamino pyrimidin-5-yl)acrylate (358 mg, 1.14 mmol) in 5 mL of N,N-diisopropylethylamine was added 191 μL of 1,8-diazabicyclo[5.4.0]undec-7-ene. The reaction mixture was heated at reflux overnight then cooled to room temperature. The resultant solid was collected by filtration and combined with the gum remaining in the flask. This combined material was purified by flash chromatography eluting with ethyl acetate to provide 176 mg (57%) of 2-methanesulfanyl-8-phenyl-8H-pyrido[2,3-d]pyrimidin-7 one, mp 176-178°C. Analysis calculated for $C_{14}H_{11}N_3OS$ 0.05 H_2O: C, 60.43; H, 4.32; N, 15.11. Found: C, 60.43; H, 3.97; N, 14.82.

EXAMPLE 99

2-Methanesulfinyl-8-phenyl-8H-pyrido[2,3-d]pyrimidin-7-one

To a room temperature solution of 2-methanesulfanyl-8-phenyl-8H-pyrido[2,3 d]pyrimidin-7-one (457 mg, 1.70 mmol) in 30 mL of chloroform was added (±)-*trans*-2-(phenylsulfonyl)-3-phenyloxaziridine (536 mg, 2.06 mmol). The solution was stirred at room temperature overnight then concentrated in vacuo. The residue was purified by flash chromatography eluting with a gradient of ethyl acetate to 10% methanol in ethyl acetate to provide 397 mg

(82%) of 2-methanesulfinyl-8-phenyl-8H-pyrido[2,3-d]pyrimidin-7-one, mp 248-250°C.

Analysis calculated for $C_{14}H_{11}N_3O_2S$ 0.02 H_2O: C, 58.21; H, 3.95; N, 14.55.

Found: C, 58.04; H, 3.91; N, 14.36.

EXAMPLE 100

2-Ethylamino-8-phenyl-8H-pyrido[2,3-d]pyrimidin-7-one

A mixture of 2-methanesulfinyl-8-phenyl-8H-pyrido[2,3-d]pyrimidin-7-one (81 mg, 0.28 mmol) and 1.5 mL of aqueous ethyl amine was stirred at room temperature for 10 minutes then partitioned between water and ethyl acetate. The organic layer was washed with saturated sodium bicarbonate and brine, dried over magnesium sulfate, filtered, and concentrated in vacuo to give 54 mg (72%) of 2-ethylamino-8-phenyl-8H-pyrido[2,3-d]pyrimidin-7-one, mp 193-195°C.

Analysis calculated for $C_{15}H_{14}N_4O$: C, 67.65; H, 5.30; N, 21.04.

Found: C, 67.48; H, 5.01; N, 20.68.

EXAMPLE 101

2-Phenylamino-8-phenyl-8H-pyrido[2,3-d]pyrimidin-7-one

A mixture of 2-methanesulfinyl-8-phenyl-8H-pyrido[2,3-d]pyrimidin-7-one (197 mg, 0.69 mmol) and 1 mL of aniline was heated at 175°C for 10 minutes then cooled to room temperature. Hexane and ethyl acetate were added, and the solid was collected by filtration and purified by flash chromatography eluting with ethyl acetate. The fractions containing product were concentrated, and the residue was recrystallized first from hexane and ethyl acetate then from chloroform and ethyl acetate to provide 85 mg (39%) of 2-phenylamino-8-phenyl-8H-pyrido[2,3-d]pyrimidin-7-one, mp 300-302°C.

Analysis calculated for $C_{19}H_{14}N_4O$ 0.25 H_2O: C, 71.59; H, 4.55; N, 17.58.

Found: C, 71.91; H, 4.39; N, 17.59.

EXAMPLE 102

4-Cyclopentylamino-2-methanesulfanyl-pyrimidine-5-carboxylic acid ethyl ester

To a room temperature solution of 4-chloro-2-methanesulfanyl-pyrimidine-5-carboxylic acid ethyl ester (12.48 g, 53.8 mmol) in 150 mL of tetrahydrofuran was added 22 mL of triethylamine followed by cyclopentylamine (6.70 g, 77.0 mmol). The solution was stirred at room temperature for 1 hour. The white solid was removed by filtration washing with ethyl acetate. The filtrate was concentrated in vacuo and partitioned between ethyl acetate and saturated aqueous sodium bicarbonate. The organic layer was washed with brine, dried over magnesium sulfate, filtered, and concentrated. A solution of 2:1 hexane:ethyl acetate was added to the residue, and the resultant white solid was collected to provide 13.3 g (88%) of 4-cyclopentylamino-2-methanesulfanyl-pyrimidine-5-carboxylic acid ethyl ester as an oil.

Analysis calculated for $C_{13}H_{19}N_3O_2S$: C, 55.49; H, 6.81; N, 14.93.
Found: C, 55.59; H, 6.72; N, 14.85.

EXAMPLE 103

(4-Cyclopentylamino-2-methanesulfanyl-pyrimidin-5-yl)-methanol

A solution of 4-cyclopentylamino-2-methanesulfanyl-pyrimidine-5-carboxylic acid ethyl ester (13.0 g, 46.3 mmol) in 50 mL of tetrahydrofuran was added dropwise to a room temperature suspension of lithium aluminum hydride (3.2 g, 84.2 mmol) in 150 mL of tetrahydrofuran. The reaction mixture was stirred at room temperature for 20 minutes, then carefully quenched with 6 mL of water, followed by 6 mL of 15% NaOH and 19 mL of water. After stirring for 1 hour, the white precipitate was removed by filtration washing with ethyl acetate. The filtrate was concentrated in vacuo, and hexane and ethyl acetate were added to the residue. Filtration of the white solid provided 8.39 g (76%) of (4-cyclopentylamino-2-methanesulfanyl-pyrimidin-5-yl)-methanol, mp 127-128°C.

Analysis calculated for $C_{11}H_{17}N_3OS$ 0.1 H_2O: C, 54.79; H, 7.19; N, 17.43.
Found: C, 54.68; H, 7.12; N, 17.23.

EXAMPLE 104

4-Cyclopentylamino-2-methanesulfanyl-pyrimidine-5-carboxaldehyde

To (4-cyclopentylamino-2-methanesulfanyl-pyrimidin-5-yl)-methanol (8.00 g, 33.5 mmol) in 400 mL of chloroform was added manganese oxide (18.5 g, 213 mmol). The suspension was stirred at room temperature overnight. An additional amount of manganese oxide (2.5 g, 29 mmol) was added, and stirring was continued for 2.5 hours. The mixture was filtered through celite washing with chloroform. The filtrate was concentrated in vacuo to give 7.93 g (99%) of 4-cyclopentylamino-2-methanesulfanyl-pyrimidine-5-carboxaldehyde as an oil.

Analysis calculated for $C_{11}H_{15}N_3OS$: C, 55.67; H, 6.37; N, 17.71.

Found: C, 55.60; H, 6.24; N, 17.70.

EXAMPLE 105

Ethyl 3-(4-Cyclopentylamino-2-methanesulfanyl-pyrimidin-5-yl)acrylate

To a room temperature solution of 4-cyclopentylamino-2-methanesulfanyl-pyrimidine-5-carboxaldehyde (7.74 g, 32.7 mmol) in 110 mL of tetrahydrofuran was added (carbethoxymethylene)triphenylphosphorane (15.0 g, 43.1 mmol). The reaction mixture was heated at reflux for 1.5 hours, then cooled to room temperature and partitioned between ethyl acetate and 1N HCl. Concentrated aqueous sodium hydroxide was added to the acid layer followed by extraction of the product into ethyl acetate. The organic layer was dried over magnesium sulfate, filtered, and concentrated in vacuo. The residue was purified by flash chromatography eluting with 4:1 hexane:ethyl acetate to provide 6.58 g (66%) of ethyl 3-(4-cyclopentylamino-2-methanesulfanyl-pyrimidin-5-yl)acrylate, mp 98-101°C.

Analysis calculated for $C_{15}H_{21}N_3O_2S$: C, 58.61; H, 6.89; N, 13.67.

Found: C, 58.57; H, 6.83; N, 13.52.

EXAMPLE 106

8-Cyclopentyl-2-methanesulfanyl-8H-pyrido[2,3-d]pyrimidin-7-one

A mixture of ethyl 3-(4-cyclopentylamino-2-methanesulfanyl-pyrimidin-5-yl)acrylate (1.42 g, 4.62 mmol) and 5 mL of 1,8-diazabicyclo[5.4.0]undec-7-ene

was heated at reflux for 30 minutes. The reaction mixture was directly purified by flash chromatography eluting with a gradient of 1:1 hexane:ethyl acetate to all ethyl acetate to provide 677 mg (56%) of 8-cyclopentyl-2-methanesulfanyl-8H-pyrido[2,3-d]pyrimidin-7-one, mp 100-102°C.

Analysis calculated for $C_{13}H_{15}N_3OS$: C, 59.75; H, 5.79; N, 16.08.

Found: C, 59.59; H, 5.71; N, 15.95.

EXAMPLE 107

8-Cyclopentyl-2-methanesulfinyl-8H-pyrido[2,3-d]pyrimidin-7-one

To a room temperature solution of 8-cyclopentyl-2-methanesulfanyl-8H-pyrido[2,3-d]pyrimidin-7-one (215 mg, 0.82 mmol) in 10 mL of chloroform was added (±)-*trans*-2-(phenylsulfonyl)-3-phenyloxaziridine (240 mg, 0.92 mmol). The solution was stirred at room temperature overnight then concentrated in vacuo. Ethyl acetate was added to the residue, and the resultant solid was collected by filtration to provide 134 mg (59%) of 8-cyclopentyl-2-methanesulfinyl-8H-pyrido[2,3-d]pyrimidin-7-one, mp 170-173°C.

Analysis calculated for $C_{13}H_{15}N_3O_2S$: C, 56.30; H, 5.45; N, 15.15.

Found: C, 56.11; H, 5.36; N, 14.91.

EXAMPLE 108

8-Cyclopentyl-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one

A mixture of 8-cyclopentyl-2-methanesulfinyl-8H-pyrido[2,3-d]pyrimidin-7-one (257 mg, 0.93 mmol) and 2 mL of aniline was heated at reflux for 20 minutes then cooled to room temperature. Most of the aniline was removed under high vacuum. The residue was purified by flash chromatography eluting with a gradient of 3:2 hexane:ethyl acetate to all ethyl acetate to provide 124 mg of product. Recrystallization from hexane and ethyl acetate gave 72 mg (26%) of 8-cyclopentyl-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one , mp 188-192°C.

Analysis calculated for $C_{18}H_{18}N_4O$ 0.3 H_2O: C, 69.34; H, 6.01; N, 17.97.

Found: C, 69.06; H, 5.78; N, 17.95.

EXAMPLES 109-271

The following invention compounds were similarly prepared by following the general procedures of the foregoing examples.

EXAMPLE 109

8-Ethyl-2-[3-(4-methyl-piperazin-1-yl)-propylamino-8H-pyrido[2,3-d]pyrimidin-7-one, mp 85-85°C.

EXAMPLE 110

8-Ethyl-2-(4-pyrrol-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one, mp 220-222°C.

EXAMPLE 111

8-Isopropyl-2-(4-methoxy-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one, mp 153-155°C.

EXAMPLE 112

2-(4-Hydroxy-phenylamino)-8-isopropyl-8H-pyrido[2,3-d]pyrimidin-7-one, mp 226-228°C.

EXAMPLE 113

2-[4-(4-Methyl-piperazin-1-yl)-phenylamino]-8-phenyl-8H-pyrido[2,3-d]pyrimidin-7-one, mp 259-262°C.

EXAMPLE 114

8-Cyclopentyl-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one, mp 175-177°C.

EXAMPLE 115

8-(3-Benzyloxy-propyl)-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one, mp 148-150°C.

EXAMPLE 116

8-(3-Benzyloxy-propyl)-2-[4-(2-diethylamino-ethoxy)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one, mp 70-72°C.

EXAMPLE 117

8-Cyclopentyl-2[4-(2-diethylamino-ethoxy)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one, mp 105-107°C.

EXAMPLE 118

2-[4-(2-Diethylamino-ethoxy)-phenylamino]-8-phenyl-8H-pyrido[2,3-d]pyrimidin-7-one, mp 165-167°C.

EXAMPLE 119

4-Cyclohexylamino-2-methylsulfanyl-pyrimidine-5-carboxylic acid ethyl ester, oil.

EXAMPLE 120

4-Cyclopropylamino-2-methylsulfanyl-pyrimidine-5-carboxylic acid ethyl ester, oil.

EXAMPLE 121

(4-Cyclohexylamino-2-methylsulfanyl-pyrimidin-5-yl)-methanol, mp 127-129°C.

EXAMPLE 122

4-Cyclohexylamino-2-methylsulfanyl-pyrimidine-5-carboxaldehyde, oil.

EXAMPLE 123

3-(4-Cyclohexylamino-2-methysulfanyl-pyrimidin-5-yl)-acrylic acid ethyl ester

EXAMPLE 124

(4-Cyclopropylamino-2-methylsulfanyl-pyrimidin-5-yl)-methanol, mp 134-135°C.

EXAMPLE 125

4-Cyclopropylamino-2-methylsulfanyl-pyrimidine-5-carboxaldehyde, mp 63-64°C.

EXAMPLE 126

8-Cyclohexyl-2-methylsulfanyl-8H-pyrido[2,3-d]pyrimidin-7-one, mp 131-132°C.

EXAMPLE 127

8-Cyclohexyl-2-methanesulfinyl-8H-pyrido[2,3-d]pyrimidin-7-one, mp 187-190°C.

EXAMPLE 128

3-(4-Cyclopropylamino-2-methylsulfanyl-pyrimidin-5-yl)-acrylic acid ethyl ester, oil.

EXAMPLE 129

8-Cyclopropyl-2-methylsulfanyl-8H-pyrido[2,3-d]pyrimidin-7-one, mp 137-139°C.

EXAMPLE 130

8-Cyclopropyl-2-methanesulfinyl-8H-pyrido[2,3-d]pyrimidin-7-one, mp 210-212°C.

EXAMPLE 131

8-Cyclohexyl-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one, mp 202-204°C.

EXAMPLE 132

8-Cyclohexyl-2-[4-(2-diethylamino-ethoxy)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one, mp 135-137°C.

EXAMPLE 133

8-Cyclohexyl-2[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one, mp 205-207°C.

EXAMPLE 134

8-Cyclopropyl-2-[4-(2-diethylamino-ethoxy)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one, mp 119-121°C.

EXAMPLE 135

8-Cyclopropyl-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one, mp 191-193°C.

EXAMPLE 136

8-Cyclopropyl-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one, mp 210-211°C.

EXAMPLE 137

8-(2-Benzyloxy-ethyl)-2-methanesulfinyl-8H-pyrido[2,3-d]pyrimidin-7-one, mp 118-120°C.

EXAMPLE 138

8-(3-Benzyloxy-propyl)-2-(4-dimethylamino-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one, mp 144-146°C.

EXAMPLE 139

8-(2-Benzyloxy-ethyl)-2-[4-(2-diethylamino-ethoxy)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one, mp 95-97°C.

EXAMPLE 140

8-(2-Benzyloxy-ethyl)-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one, mp 183-185°C.

EXAMPLE 141

8-Isopropyl-2-[4-(2-morpholin-4-yl-ethoxy)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one, mp 118-119°C.

EXAMPLE 142

8-Cyclohexyl-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one, mp 198-200°C.

EXAMPLE 143

8-Cyclohexyl-2-{4-[4-(2-hydroxy-ethyl)-3,5-dimethyl-piperazin-1-yl]-phenylamino}-8H-pyrido[2,3-d]pyrimidin-7-one, mp 175-177°C.

EXAMPLE 144

8-Cyclohexyl-2-{4-[4-(3-dimethylamino-propyl)-piperazin-1-yl]-phenylamino}-8H-pyrido[2,3-d]pyrimidin-7-one, mp 169-170°C.

EXAMPLE 145

8-Cyclohexyl-2-[4-(3,5-dimethyl-piperazin-1-yl)-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one, mp 237-239°C.

EXAMPLE 146

4-Cycloheptylamino-2-methylsulfanyl-pyrimidine-5-carboxylic acid ethyl ester

EXAMPLE 147

8-Cyclohexyl-2-(4-dimethylamino-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one, mp 204-205°C.

EXAMPLE 148

8-Cyclohexyl-2-(4-fluoro-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one, mp 209-211°C.

EXAMPLE 149

(4-Cycloheptylamino-2-methylsulfanyl-pyrimidin-5-yl)-methanol, mp 141-143°C.

EXAMPLE 150

8-Cyclohexyl-2-[4-(2-diethylamino-ethoxy)-3-methyl-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one, mp 119-121°C.

EXAMPLE 151

8-Cycloheptyl-2-methylsulfanyl-8H-pyrido[2,3-d]pyrimidin-7-one, mp 135-136°C.

EXAMPLE 152

8-Cycloheptyl-2-methanesulfinyl-8H-pyrido[2,3-d]pyrimidin-7-one, mp 183-184°C.

EXAMPLE 153

8-Cyclohexyl-2-cyclohexylamino-8H-pyrido[2,3-d]pyrimidin-7-one, mp 169-170°C.

EXAMPLE 154

2-[4-(2-Diethylamino-ethoxy)-phenylamino]-8-[3-(tetrahydro-pyran-2-yloxy)-propyl]-8H-pyrido[2,3-d]pyrimidin-7-one, mp 102-104 C.

EXAMPLE 155

8-Cycloheptyl-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one, mp 156-158°C.

EXAMPLE 156

8-Cycloheptyl-2-[4-(2-diethylamino-ethoxy)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one, mp 121-122°C.

EXAMPLE 157

8-Cyclopentyl-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one, mp 198-199°C.

EXAMPLE 158

2-(4-Piperidin-1-yl-phenylamino)-8-[3-(tetrahydro-pyran-2-yloxy)-propyl]-8H-pyrido[2,3-d]pyrimidin-7-one, mp 85-86°C.

EXAMPLE 159

8-Cyclohexyl-2-[4-(4-methyl-piperidin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one, mp 208-209°C.

EXAMPLE 160

8-Cyclohexyl-2-(4-pyrrolidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one, mp 199-200°C.

EXAMPLE 161

8-Cyclohexyl-2-(4-pyrrole-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one, mp 183-184°C.

EXAMPLE 162

8-Cyclohexyl-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one, mp 241-242°C.

EXAMPLE 163

8-Cycloheptyl-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one, mp 201-202°C.

EXAMPLE 164

1-[4-(8-Cyclohexyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-phenyl]-piperidine-4-carboxylic acid ethyl ester, mp 174-175°C.

EXAMPLE 165

8-Cyclohexyl-2-(2-piperidin-1-yl-ethylamino)-8H-pyrido[2,3-d]pyrimidin-7-one, mp 156-157°C.

EXAMPLE 166

8-Cyclohexyl-2-(3-piperidin-1-yl-propylamino)-8H-pyrido[2,3-d]pyrimidin-7-one, mp 111-112°C.

EXAMPLE 167

8-Cyclohexyl-2-[4-(3,5-dimethyl-piperidin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one, mp 238-240°C.

EXAMPLE 168

1-(4-Nitro-phenyl)-pyrrolidine-2-carboxylic acid tert-butyl ester (S), mp 103-104°C.

EXAMPLE 169

1-(4-Amino-phenyl)-pyrrolidine-2-carboxylic acid tert-butyl ester (S), mp 75-76°C.

EXAMPLE 170

1-[4-(8-Cyclohexyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-phenyl]-pyrrolidine-2-carboxylic acid tert-butyl ester, mp 144-145°C.

EXAMPLE 171

8-Cyclohexyl-2-[4-(3,4-dihydro-1H-isoquinolin-2-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one, mp 185°C.

EXAMPLE 172

[1-(4-Nitro-phenyl)-piperidin-3-yl]-methanol (racemic), mp 99-100°C.

EXAMPLE 173

[1-(4-Amino-phenyl)-piperidin-3-yl]-methanol (racemic), mp 108-110°C.

EXAMPLE 174

[4-(Bicyclo[2.2.1]hept-2-ylamino)-2-methylsulfanyl-pyrimidin-5-yl]-methanol (exo), mp 117-118°C.

EXAMPLE 175

8-Cyclohexyl-2-[4-(3-methyl-piperidin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one, mp 189-190°C.

EXAMPLE 176

8-Bicyclo[2.2.1]hept-2-yl-2-methylsulfanyl-8H-pyrido[2,3-d]pyrimidin-7-one (exo), mp 102-103°C.

EXAMPLE 177

8-Cyclohexyl-2-(4-thiomorpholin-4-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one, mp 213-214°C.

EXAMPLE 178

8-Bicyclo[2.2.1]hept-2-yl-2-methanesulfinyl-8H-pyrido[2,3-d]pyrimidin-7-one, mp 167-168°C.

EXAMPLE 179

8-Cyclohexylmethyl-2-methanesulfinyl-8H-pyrido[2,3-d]pyrimidin-7-one, mp 164-165°C.

EXAMPLE 180

8-Bicyclo[2.2.1]hept-2-yl-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one (exo), mp 225-226°C.

EXAMPLE 181

8-Bicyclo[2.2.1]hept-2-yl-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one (exo), mp 243-244°C.

EXAMPLE 182

8-Cyclohexylmethyl-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one, mp 230-231°C.

EXAMPLE 183

8-Cyclohexylmethyl-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one, mp 212-213°C.

EXAMPLE 184

8-Cycloheptyl-2-(4-fluoro-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one, mp 198-199°C.

EXAMPLE 185

8-Cyclohexyl-2-[4-(3-hydroxymethyl-piperidin-1-yl)-phenylamio]-8H-pyrido[2,3-d]pyrimidin-7-one, mp 194-195°C.

EXAMPLE 186

2-[1-(4-Nitro-phenyl)-piperidin-4-yl]-ethanol, mp 60-61°C.

EXAMPLE 187

3-[1-(4-Nitro-phenyl)-piperidin-4-yl]-propan-1-ol, mp 166-167°C.

EXAMPLE 188

2-[1-(4-Amino-phenyl)-piperidin-4-yl]-ethanol, mp 121-122°C.

EXAMPLE 189

3-[1-(4-Amino-phenyl)-piperidin-4-yl]-propan-1-ol, mp 98-99°C.

EXAMPLE 190

8-Cyclopentyl-2-(4-pyrrol-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one, mp 189-190°C.

EXAMPLE 191

8-Cyclopentyl-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one, mp 197-198°C.

EXAMPLE 192

[1-(4-Nitro-phenyl)-piperidin-2-yl]-methanol, mp 68-69°C.

EXAMPLE 193

1-(4-Nitro-phenyl)-piperidin-4-ol, mp 99-100°C.

EXAMPLE 194

1-(4-Amino-phenyl)-piperidin-4-ol, mp 168-169°C.

EXAMPLE 195

8-Cyclopentyl-2-[4-(3,5-dimethyl-pyrazol-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one, mp 169-171°C.

EXAMPLE 196

8-Cyclopentyl-2-{4-[4-(2-hydroxy-ethyl)-piperidin-1-yl]-phenylamino}-8H-pyrido[2,3-d]pyrimidin-7-one, mp 199-200°C.

EXAMPLE 197

8-Cyclopentyl-2-{4-[4-(3-hydroxy-propyl)-piperidin-1-yl]-phenylamino}-8H-pyrido[2,3-d]pyrimidin-7-one, mp 208-209°C.

EXAMPLE 198

8-Cyclopentyl-2-[4-(4-hydroxy-piperidin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one, mp 216-217°C.

EXAMPLE 199

[1-(4-Amino-phenyl)-piperidin-2-yl]-methanol, mp 91-92°C.

EXAMPLE 200

2-(4-Piperidin-1-yl-phenylamino)-8-(tetrohydro-furan-3-yl)-8H-pyrido[2,3-d]pyrimidin-7-one (racemic), mp 181-182°C.

EXAMPLE 201

8-Cycloheptyl-2-(3-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one, mp 123-124°C.

EXAMPLE 202

8-Cyclopentyl-2-(3-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one, mp 90-91°C.

EXAMPLE 203

8-Cyclohexyl-2-(3-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one, mp 164-165°C.

EXAMPLE 204

1-(4-Nitro-phenyl)-piperidin-3-ol, mp 112-113C.

EXAMPLE 205

1-(4-Amino-phenyl)-piperidin-3-ol, mp 101-102C.

EXAMPLE 206

8-Cyclopentyl-2-[4-(3-hydroxy-piperidin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one, mp 178-179°C.

EXAMPLE 207

8-Cyclopentyl-2-[4-(2-hydroxymethyl-piperidin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one, mp 135-136°C.

EXAMPLE 208

Dimethyl-[1-(4-nitro-phenyl)-piperidin-4-yl]-amine, mp 102-103°C.

EXAMPLE 209

1′-(4-Nitro-phenyl)-[1,4′]bipiperidinyl, mp 90-91°C.

EXAMPLE 210

[1-(4-Amino-phenyl)-piperidin-4-yl]-dimethyl-amine, mp 126-127°C.

EXAMPLE 211

2-(4-Piperidin-1-yl-phenylamino)-8-(tetrahydro-pyran-4-yl)-8H-pyrido[2,3-d]pyrimidin-7-one, mp 254-255°C.

EXAMPLE 212

8-Bicyclo[2.2.1]hept-2-yl-2-(4-fluoro-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one (exo), mp 219-220°C.

EXAMPLE 213

8-Bicyclo[2.2.1]hept-2-yl-2-[3-(1,1,2,2-tetrafluoro-ethoxy)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one (exo), mp 192°C.

EXAMPLE 214

8-Bicyclo[2.2.1]hept-2-yl-2-{4-[4-(3-hydroxy-propyl)-piperidin-1-yl]-phenylamino}-8H-pyrido[2,3-d]pyrimidin-7-one (exo), mp 223°C.

EXAMPLE 215

8-Cyclohexyl-2-[4-(4-hydroxy-piperidin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one, mp 224-225°C.

EXAMPLE 216

8-Cyclohexyl-2-{4-[4-(2-hydroxy-ethyl)-piperidin-1-yl]-phenylamino}-8H-pyrido[2,3-d]pyrimidin-7-one, mp 236-237°C.

EXAMPLE 217

8-Bicyclo[2.2.1]hept-2-yl-2-[4-[4-(3-morpholin-4-yl-propyl)-piperidin-1-yl]-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one (exo), mp 185-186°C.

EXAMPLE 218

8-Bicyclo[2.2.1]hept-2-yl-2-(4-pyrazol-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one (exo), mp 234-235°C.

EXAMPLE 219

8-Bicyclo[2.2.1]hept-2-yl-2-[4-(1,1,2,2-tetrafluoro-ethoxy)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one (exo), mp 214-215°C.

EXAMPLE 220

8-Bicyclo[2.2.1]hept-2-yl-2-(3,4-difluoro-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one (exo), mp 227-228°C.

EXAMPLE 221

8-Bicyclo[2.2.1]hept-2-yl-2-(4-trifluoromethylsulfanyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one (exo), mp 205-206°C.

EXAMPLE 222

2-Benzylamino-8-cyclohexyl-8H-pyrido[2,3-d]pyrimidin-7-one, mp 183-184°C.

EXAMPLE 223

8-Bicyclo[2.2.1]hept-2-yl-2-(biphenyl-4-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one (exo), mp 255-257°C.

EXAMPLE 224

8-Bicyclo[2.2.1]hept-2-yl-2-[4-(2-diethylamino-ethoxy)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one, mp 133-134°C.

EXAMPLE 225

8-Cyclohexyl-2-(4-methoxy-benzylamino)-8H-pyrido[2,3-d]pyrimidin-7-one, mp 165°C.

EXAMPLE 226

2-Amino-8-cyclohexyl-8H-pyrido[2,3-d]pyrimidin-7-one, mp 155°C.

EXAMPLE 227

8-Bicyclo[2.2.1]hept-2-yl-2-[4-(4-hydroxy-piperidin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one (exo), mp 206°C.

EXAMPLE 228

8-Bicyclo[2.2.1]hept-2-yl-2-{4-[4-(2-hydroxy-ethyl)-piperidin-1-yl]-phenylamino}-8H-pyrido[2,3-d]pyrimidin-7-one (exo), mp 202°C.

EXAMPLE 229 184825 (57958x123)

8-Bicyclo[2.2.1]hept-2-yl-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one (endo), mp 209°C.

EXAMPLE 230

8-Bicyclo[2.2.1]hept-2-yl-2-{4-[4-(3-dimethylamino-propyl)-piperazin-1-yl]-phenylamino}-8H-pyrido[2,3-d]pyrimidin-7-one (exo), mp 212-213°C.

EXAMPLE 231

8-Bicyclo[2.2.1]hept-2-yl-2-[4-(3-hydroxymethyl-piperidin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one (exo), mp 152°C.

EXAMPLE 232

2-Methylsulfonyl-8-[3-(tetrahydro-pyran-2-yloxy)propyl]-8H-pyrido[2,3-d]pyrimidin-7-one, mp 65-67°C.

EXAMPLE 233

2-Methylsulfinyl-8-[3-(tetrahydro-pyran-2H-yloxy)-propyl]-8H-pyrido[2,3-d]pyrimidin-7-one, mp 121-122°C.

EXAMPLE 234

8-(3-Benzyloxy-propyl)-2-(4-piperidin-1-yl)-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one, mp 148-150°C.

EXAMPLE 235

8-Bicyclo[2.2.1]hept-2-yl-2-{4-[4-(3-morpholin-4-yl-propyl)-piperidin-1-yl]-phenylamino}-8H-pyrido[2,3-d]pyrimidin-7-one, mp 197-198°C.

EXAMPLE 236

8-Bicyclo[2.2.1]hept-2-yl-2-{4-[3-(3-hydroxy-propy)-piperidin-1-yl]-phenylamino}-8H-pyrido[2,3-d]pyrimidin-7-one, mp 150-151°C.

EXAMPLE 237

8-Bicyclo[2.2.1]hept-2-yl-2-[4-(3-diethylamino-2-hydroxy-propoxy)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one, oil.

EXAMPLE 238

3-{4-[2-(tert-Butyl-dimethyl-silanyloxy)-cyclopentylamino]-2-methylsulfanyl-pyrimidin-5-yl}-acrylic acid ethyl ester. MS (CI) m/z 438 (M^+).

EXAMPLE 239

8-[2-(tert-Butyl-dimethyl-silanyloxy)-cyclopentyl]-2-methylsulfanyl-8H-pyrido[2,3-d]pyrimidin-7-one. MS (CI) m/z 392 (M + 1).

EXAMPLE 240

8-[2-(tert-Butyl-dimethyl-silanyloxy)-cyclopentyl]-2-methylsulfinyl-8H-pyrido[2,3-d]pyrimidin-7-one, mp 119-122°C.

EXAMPLE 241

8-[2-(tert-Butyl-dimethyl-silanyloxy)-cyclopentyl]-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one. MS (CI) m/z 520 (M+1).

EXAMPLE 242

8-(2-Hydroxy-cyclopentyl)-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one, mp 230-232°C.

EXAMPLE 243

4-[5-(2-Ethoxycarbonyl-vinyl)-2-methylsulfanyl-pyrimidin 4 yl amino]-piperidine-1-carboxylic acid ethyl ester, oil. MS (CI) m/z 395 (M+1).

EXAMPLE 244

4-(2-Methanesulfanyl-7-oxo-7H-pyrido[2,3-d]pyrimidin-8-yl)-piperidine-1-carboxylic acid ethyl ester, mp 165-167°C.

EXAMPLE 245

4-(2-Methanesulfinyl-7-oxo-7H-pyrido[2,3-d]pyrimidin-8-yl)-piperidine-1-carboxylic acid ethyl ester, mp 151-154°C. MS (CI) m/z 365 (M+1).

EXAMPLE 246

4-[7-Oxo-2-(4-piperidin-1-yl-phenylamino)-7H-pyrido[2,3-d]pyrimidin-8-yl]-piperidine-1-carboxylic acid ethyl ester, mp 231-233°C.

EXAMPLE 247

8-(3-Hydroxy-propyl)-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one hydrochloride salt, mp discolors at 90°C, >250°C.

EXAMPLE 248

2-(3-Bromo-2,2-dimethyl-propoxy)-tetrahydro-pyran, oil.

EXAMPLE 249

2-Methylsulfanyl-8-[2,2-dimethyl-3-(tetrahydro-pyran-2-yloxy)propyl]-8H-pyrido[2,3-d]pyrimidin-7-one, oil. MS (CI) m/z 364 (M+1).

EXAMPLE 250

2-Methylsulfinyl-8-[2,2-dimethyl-3-(tetrahydro-pyran-2-yloxy)propyl]-8H-pyrido[2,3-d]pyrimidin-7-one, oil.

EXAMPLE 251

8-(2,2-Dimethyl-2-(tetrahydro-pyran-2-yloxy)propyl]-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one, oil.

EXAMPLE 252

8-(Bicyclo[2.2.1]hept-2-yl-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one (exo), mp 233-234°C.

EXAMPLE 253

8-(Bicyclo[2.2.1]hept-2-yl-2-[4-(2-hydroxymethyl-piperidin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one (exo), mp 160-161°C.

EXAMPLE 254

8-(Bicyclo[2.2.1]hept-2-yl-2-[4-(3-hydroxy-piperidin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one, mp 218°C.

EXAMPLE 255

8-(Bicyclo[2.2.1]hept-2-yl-2-[4-(3,5-dimethyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one, mp 245-246°C.

EXAMPLE 256

2-(3,4-Dimethoxy-benzylamino)-8-isopropyl-8H-pyrido[2,3-d]pyrimidin-7-one, mp 128°C.

EXAMPLE 257

2-Amino-8-isopropyl-8H-pyrido[2,3-d]pyrimidin-7-one, mp 153°C.

EXAMPLE 258

8-Cyclohexyl-2-{4-[4-(2-morpholin-4-yl-ethyl)-piperidin-1-yl]-phenylamino}-8H-pyrido[2,3-d]pyrimidin-7-one, mp 245-246°C.

EXAMPLE 259

8-Bicyclo[2.2.1]hept-2-yl-2-[4-[4-(2-morpholin-4-yl-ethyl)-piperidin-1-yl]-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one (exo), mp 223-224°C.

EXAMPLE 260

8-Isopropyl-2-{4-[4-(3-morpholin-4-yl-propyl)-piperidin-1-yl]-phenylamino}-8H-pyrido[2,3-d]pyrimidin-7-one, mp 195-196°C.

EXAMPLE 261

8-Bicyclo[2.2.1]hept-2-yl-2-[4-(2-hydroxy-3-morpholin-4-yl-propoxy)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one, oil.

EXAMPLE 262

8-Bicyclo[2.2.1]hept-2-yl-2-{4-[3-(3-morpholin-4-yl-propyl)-piperidin-1-yl]-phenylamino}-8H-pyrido[2,3-d]pyrimidin-7-one, mp 156-157°C.

EXAMPLE 263

8-Bicyclo[2.2.1]hept-2-yl-2-[4-(3-morpholin-4-ylmethyl-piperidin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one, mp 155-157°C.

EXAMPLE 264

8-Ethyl-6-methyl-2-{4-[4-(3-morpholin-4-yl-propyl)-piperidin-1-yl]-phenylamino}-8H-pyrido[2,3-d]pyrimidin-7-one, mp 199-200°C.

EXAMPLE 265

8-Bicyclo[2.2.1]hept-2-yl-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one, oil.

EXAMPLE 266

8-Cyclohexyl-6-methyl-2-{4-[4-(3-morpholin-4-yl-propyl)-piperidin-1-yl]-phenylamino}-8H-pyrido[2,3-d]pyrimidin-7-one

EXAMPLE 267

6-Amino-8-cyclohexyl-2-{4-[4-(3-morpholin-4-yl-propyl)-piperidin-1-yl]-phenylamino}-8H-pyrido[2,3-d]pyrimidin-7-one

EXAMPLE 268

4-Amino-8-cyclohexyl-2-{4-[4-(3-morpholin-4-yl-propyl)-piperidin-1-yl]-phenylamino}-8H-pyrido[2,3-d]pyrimidin-7-one

EXAMPLE 269

5-Amino-8-cyclohexyl-2-{4-[4-(3-morpholin-4-yl-propyl)-piperidin-1-yl]-phenylamino}-8H-pyrido[2,3-d]pyrimidin-7-one

EXAMPLE 270

8-Cyclohexyl-4-hydroxy-2-{4-[4-(3-morpholin-4-yl-propyl)-piperidin-1-yl]-phenylamino}-8H-pyrido[2,3-d]pyrimidin-7-one

EXAMPLE 271

8-Cyclohexyl-6-fluoro-2-{4-[4-(3-morpholin-4-yl-propyl)-piperidin-1-yl]-phenylamino}-8H-pyrido[2,3-d]pyrimidin-7-one

EXAMPLE 272

8-Butyl-2-methylsufanyl-8H-pyrido[2,3-d]pyrimidin-7-one

2-Methylsulfanyl-8H-pyrido[2,3-d]pyrimidin-7-one (1.005 g, 5.2 mmol) was mixed with n-butyl bromide (650 μL, 5.7 mmol) and tetramethyl guanidine (1 mL, 7.8 mmol) in 20 mL of DMF under nitrogen. The mixture was stirred for 8 hours. The reaction mixture was diluted with 100 mL of ethyl acetate, extracted with saturated $NaHCO_3$ solution and subsequently with brine. The organic layer was separated, dried over anhydrous Na_2SO_4, and evaporated to dryness. The crude product was purified by chromatography (silica gel, 30% ethyl acetate: hexane) to give the title compound 1.153 g (89%). MS (CI) 250 MH^+.

EXAMPLE 273

8-Butyl-2-chloro-8H-pyrido[2,3-d]pyrimidin-7-one

A solution of the product from Example 272 (1.25 g, 5 mmol) in 30 mL of $CHCl_3$ and 50 μL ethyl alcohol was treated with SO_2Cl_2 (700 μL, 8.12 mmol). The reaction mixture was stirred for 18 hours at room temperature. The crude mixture was poured into 100 mL of water. The organic layer was collected. The aqueous layer was further extracted with two 20 mL portions of ethyl acetate. The combined organic layers were dried over anhydrous Na_2SO_4 and evaporated to dryness. The crude product was purified by chromatography (silica gel, 30% ethyl acetate:hexane) to give the title compound 0.6 g (50%). MS (CI) 238 MH^+.

EXAMPLE 274

2-Methylsulfanyl-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one

The title compound was prepared from 2-methylsulfanyl-8H-pyrido[2,3-d]pyrimidin-7-one (10 g, 51.7 mmol) and iodopropane (5.5 mL, 57 mmol) by using the procedure described in Example 272 (Yield 97%). MS(CI) 236 MH^+.

EXAMPLE 275

2-Chloro-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one

The title compound was prepared from the product of Example 274 using the procedure described in Example 273 (Yield 44%). MS (CI) 224 MH^+. Analysis calculated for $C_{10}H_{10}ClN_3O$ 0.04 H_2O: C, 53.53; H, 4.53; N, 18.73; H_2O, 0.32. Found: C, 53.47; H, 4.37; N, 18.55; H_2O, 0.69.

EXAMPLE 276

8-(1-Ethyl-propyl)-2-methylsufanyl-8H-pyrido[2,3-d]pyrimidin-7-one

The title compound was prepared from 2-methylsulfanyl-8H-pyrido[2,3-d]pyrimidin-7-one (10 g, 51.7 mmol) and 3-bromopentane (6.5 mL, 52 mmol) by using the procedure described in Example 272 (Yield 44%). MS (CI) 264.0 MH^+.

EXAMPLE 277

8-Cyclopentyl-2-methylsufanyl-8H-pyrido[2,3-d]pyrimidin-7-one

The title compound was prepared from 2-methylsulfanyl-8H-pyrido[2,3-d]pyrimidin-7-one (10 g, 51.7 mmol) and bromo cyclopentane (5.6 mL, 52 mmol) by using the procedure described in Example 272 (Yield 50%). MS (CI) 262.0 MH^+.

EXAMPLE 278

8-Cyclopropyl-2-methylsufanyl-8H-pyrido[2,3-d]pyrimidin-7-one

The title compound was prepared from 2-methylsulfanyl-8H-pyrido[2,3-d]pyrimidin-7-one (3 g, 15.5 mmol) and bromomethyl cyclopropane (1.6 mL, 16 mmol) by using the procedure described in Example 272.

EXAMPLE 279

2-Methylsulfanyl-8-(2,2,2-trifluoroethyl)-8H-pyrido[2,3-d]pyrimidin-7-one

The title compound was prepared from 2-methylsulfanyl-8H-pyrido[2,3-d]pyrimidin-7-one (3 g, 15.5 mmol) and 1,1,1-trifluoro iodoethane (1.6 mL, 16 mmol) by using the procedure described in Example 272 (Yield 19%). MS (CI) 275.9 MH^+.

EXAMPLE 280

2-Chloro-8-methyl-8H-pyrido[2,3-d]pyrimidin-7-one

The title compound was prepared from Example 26 (3.3 g, 13.2 mmol) using the procedure described in Example 273 (Yield 77%). MS (CI) 196.0 MH^+.

EXAMPLE 281

2-Chloro-8-(1-ethylpropyl)-8H-pyrido[2,3-d]pyrimidin-7-one

The title compound was prepared from Example 276 (10 g, 38 mmol) by using the procedure described in Example 273 (Yield 53%). MS (CI) 252 MH^+.

EXAMPLE 282

2-Chloro-8-cyclopentyl-8H-pyrido[2,3-d]pyrimidin-7-one

The title compound was prepared from Example 277 (5.5 g, 21 mmol) by using the procedure described in Example 273 (Yield 57%). MS (CI) 250 MH^+.

EXAMPLE 283

2-Chloro-8-cyclopropylmethyl-8H-pyrido[2,3-d]pyrimidin-7-one

The title compound was prepared from Example 278 (2 g, 8 mmol) by using the procedure described in Example 273.

EXAMPLE 284

2-Chloro-8-(2,2,2-trifluoroethyl)-8H-pyrido[2,3-d]pyrimidin-7-one

The title compound was prepared from Example 279 (1.7 g, 6.2 mmol) by using the procedure described in Example 273 (Yield 92%). MS (CI) 263.6 MH^+.

EXAMPLE 285

8-Methyl-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one

A solution of 2-chloro-8-methyl-8H-pyrido[2,3-d]pyrimidin-7-one (0.05 mmol) and aniline (0.15 mmol) in 500 μL of dioxane was heated at 100°C on an orbital shaker for 72 hours. The reaction mixture was cooled to room temperature and concentrated under a stream of nitrogen. The residue was purified by preparative HPLC. Preparative HPLC separations were achieved using a 30 mm ID × 10 cm C-18 YMC column (Waters, Milford, MA). The column flow

was set to 25 mL/min for chromatography and 16 mL/min for column equilibration. The mobile phase is a binary acetonitrile/water system buffered with 0.05% trifluoroacetic acid. Initial chromatographic conditions are set at 10% acetonitrile. Separation of samples is achieved with a gradient of 10% to 100% acetonitrile over 6.5 minutes with a hold at 100% acetonitrile for an additional 3.5 minutes. The eluent was concentrated to give the title compound.
MS (CI) 253 MH^+.

EXAMPLES 286-621

The following compounds were similarly prepared by utilizing the general procedure described in Example 285.

EXAMPLE 286

8-Ethyl-2-(1H-indazol-5-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one
MS (CI) 307 MH^+.

EXAMPLE 287

2-(1H-Benzotriazol-5-ylamino)-8-ethyl-8H-pyrido[2,3-d]pyrimidin-7-one
MS (CI) 308 MH^+.

EXAMPLE 288

[4-(8-Ethyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-phenyl]-carbamic acid tert-butyl ester MS (CI) 382 MH^+.

EXAMPLE 289

8-Ethyl-2-(2-fluoro-4-hydroxy-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 301 MH^+.

EXAMPLE 290

2-(3-Chloro-4-hydroxy-phenylamino)-8-ethyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 317 MH^+.

EXAMPLE 291

2-(3,5-Dichloro-4-hydroxy-phenylamino)-8-ethyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 351 MH^+.

EXAMPLE 292

8-Ethyl-2-(3,4,5-trimethoxy-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 357 MH^+.

EXAMPLE 293

8-Ethyl-2-(4-fluoro-3-trifluoromethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 353 MH^+.

EXAMPLE 294

8-Ethyl-2-(4-fluoro-3-methyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 299 MH^+.

EXAMPLE 295

4-(8-Ethyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-benzenesulfonamide MS (CI) 346 MH^+.

EXAMPLE 296

2-(3-Hydroxy-4-methoxy-phenylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 319 MH^+.

EXAMPLE 297

8-Ethyl-2-(2-fluoro-5-nitro-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) MH^+.

EXAMPLE 298

4-(8-Ethyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-phthalonitrile MS (CI) 317 MH^+.

EXAMPLE 299

N-[2-Cyano-5-(8-ethyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-phenyl]-acetamide MS (CI) 349 MH^+.

EXAMPLE 300

8-Ethyl-2-(3-methoxy-5-trifluoromethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 365 MH^+.

EXAMPLE 301

2-(3,4-Difluoro-phenylamino)-8-ethyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 303 MH^+.

EXAMPLE 302

8-Ethyl-2-(2-fluoro-5-trifluoromethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 353 MH^+.

EXAMPLE 303

2-(3,5-Difluoro-phenylamino)-8-ethyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 303 MH^+.

EXAMPLE 304

4-(8-Ethyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-benzonitrile MS (CI) 292 MH^+.

EXAMPLE 305

8-Ethyl-2-(3-trifluoromethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 335 MH^+.

EXAMPLE 306

2-(3-Bromo-4-trifluoromethoxy-phenylamino)-8-ethyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 429 MH^+.

EXAMPLE 307

N-[5-(8-Ethyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-2-methyl-phenyl]-methanesulfonamide MS (CI) 374 MH^+.

EXAMPLE 308

N-[2-Cyano-4-(8-ethyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-phenyl]-acetamide MS (CI) 349 MH^+.

EXAMPLE 309

2-Phenylamino-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 281 MH^+.

EXAMPLE 310

2-(3-Chloro-4-methoxy-phenylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 345 MH^+.

EXAMPLE 311

2-(2-Fluoro-5-trifluoromethyl-phenylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 367 MH.

EXAMPLE 312

2-(4-Chloro-3-trifluoromethyl-phenylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 383 MH^+.

EXAMPLE 313

8-Propyl-2-(3-trifluoromethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 349 MH^+.

EXAMPLE 314

2-(4-Bromo-3-trifluoromethyl-phenylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 427, 429 MH^+.

EXAMPLE 315

2-(3,5-Bis-trifluoromethyl-phenylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 417 MH^+.

EXAMPLE 316

2-(3-Iodo-phenylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one

MS (CI) 407 MH^+.

EXAMPLE 317

4-(7-Oxo-8-propyl-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-benzenesulfonamide MS (CI) 360 MH^+.

EXAMPLE 318

2-(3,4-Dimethyl-phenylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one

MS (CI) 309 MH^+.

EXAMPLE 319

2-(3,5-Dichloro-phenylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one

MS (CI) 349 MH^+.

EXAMPLE 320

2-(2-Fluoro-4-nitro-phenylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one

MS (CI) 344 MH^+.

EXAMPLE 321

2-(2,4-Difluoro-phenylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one

MS (CI) 317 MH^+.

EXAMPLE 322

4-(7-Oxo-8-propyl-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-benzonitrile MS (CI) 306 MH^+.

EXAMPLE 323

2-(1H-Indol-5-ylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one

MS (CI) 320 MH^+.

EXAMPLE 324

2-(1H-Indazol-5-ylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one

MS (CI) 321 MH^+.

EXAMPLE 325

2-(1H-Benzotriazol-5-ylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 322 MH^+.

EXAMPLE 326

[4-(7-Oxo-8-propyl-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-phenyl]-carbamic acid tert-butyl ester MS (CI) 408 MH^+.

EXAMPLE 327

2-(3-Chloro-4-hydroxy-phenylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 331 MH^+.

EXAMPLE 328

2-(3,5-Dichloro-4-hydroxy-phenylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 365 MH^+.

EXAMPLE 329

2-(4-Methoxy-phenylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 311 MH^+.

EXAMPLE 330

2-(3-Nitro-phenylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 326 MH^+.

EXAMPLE 331

2-(3,4-Dimethoxy-phenylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 341 MH^+.

EXAMPLE 332

2-(4-Fluoro-phenylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 299 MH^+.

EXAMPLE 333

2-(2-Fluoro-5-nitro-phenylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 344 MH^+.

EXAMPLE 334

8-Propyl-2-(3,4,5-trimethoxy-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 371 MH^+.

EXAMPLE 335

2-(4-Fluoro-3-trifluoromethyl-phenylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 367 MH^+.

EXAMPLE 336

2-(3-Hydroxy-4-methoxy-phenylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 327 MH^+.

EXAMPLE 337

2-(4-Fluoro-3-methyl-phenylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 313 MH^+.

EXAMPLE 338

2-(3-Fluoro-4-methoxy-phenylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 329 MH^+.

EXAMPLE 339

4-(7-Oxo-8-propyl-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-phthalonitrile MS (CI) 331 MH^+.

EXAMPLE 340

N-[2-Cyano-5-(7-oxo-8-propyl-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-phenyl]-acetamide MS (CI) 363 MH^+.

EXAMPLE 341

2-(4-Bromo-3-chloro-phenylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 393 MH^+.

EXAMPLE 342

2-(3-Methoxy-5-trifluoromethyl-phenylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 379 MH^+.

EXAMPLE 343

2-(3,4-Difluoro-phenylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 317 MH^+.

EXAMPLE 344

2-(3-Chloro-4-iodo-phenylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 441 MH^+.

EXAMPLE 345

N-Methyl-N-[4-(7-oxo-8-propyl-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-phenyl]-acetamide MS (CI) 352 MH^+.

EXAMPLE 346

2-(3,5-Dimethyl-phenylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 309 MH^+.

EXAMPLE 347

2-(3-Chloro-4-methyl-phenylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 329 MH^+.

EXAMPLE 348

3-(7-Oxo-8-propyl-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-benzenesulfonamide MS (CI) 360 MH^+.

EXAMPLE 349

2-(3,5-Difluoro-phenylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one

MS (CI) 317 MH^+.

EXAMPLE 350

2-(3,4-Dichloro-phenylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 349 MH^+.

EXAMPLE 351

2-(4-Fluoro-3-nitro-phenylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 344 MH^+.

EXAMPLE 352

2-(2,3-Dihydro-1H-indol-6-ylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 322 MH^+.

EXAMPLE 353

N-[3-(7-Oxo-8-propyl-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-phenyl]-acetamide MS (CI) 338 MH^+.

EXAMPLE 354

2-(4-Hydroxy-3-methyl-phenylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 311 MH^+.

EXAMPLE 355

2-(4-Hydroxy-3-morpholin-4-ylmethyl-phenylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 396 MH^+.

EXAMPLE 356

2-(2,3-Dimethyl-2,3-dihydro-1H-indol-5-ylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 349 MH^+.

EXAMPLE 357

2-(2,3-Dihydro-1H-indol-5-ylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 321 MH^+.

EXAMPLE 358

2-(1H-Indazol-6-ylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 321 MH^+.

EXAMPLE 359

8-Propyl-2-(3,4,5-trifluoro-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 335 MH^+.

EXAMPLE 360

2-(4-Bromo-3-methyl-phenylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 373 MH^+.

EXAMPLE 361

8-Propyl-2-(4-trifluoromethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 349 MH^+.

EXAMPLE 362

8-Propyl-2-(4-trifluoromethoxy-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 365 MH^+.

EXAMPLE 363

2-(3-Bromo-4-trifluoromethoxy-phenylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 443 MH^+.

EXAMPLE 364

8-Butyl-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 295 MH^+.

EXAMPLE 365

8-Butyl-2-(3-chloro-4-methoxy-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 359 MH^+.

EXAMPLE 366

8-Butyl-2-(2,4,6-trifluoro-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one

MS (CI) 349 MH^+.

EXAMPLE 367

8-Butyl-2-(2-fluoro-4-nitro-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 359 MH^+.

EXAMPLE 368

8-Butyl-2-(2,4-difluoro-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 331 MH^+.

EXAMPLE 369

2-(3-Chloro-4-fluoro-phenylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 333 MH^+.

EXAMPLE 370

N-[4-(8-Butyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-phenyl]-N-methyl-acetamide MS (CI) 366 MH^+.

EXAMPLE 371

4-(8-Butyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-benzamide MS (CI) 339 MH^+.

EXAMPLE 372

8-Butyl-2-(2-fluoro-5-trifluoromethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 381 MH^+.

EXAMPLE 373

8-Butyl-2-(3-trifluoromethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 363 MH^+.

EXAMPLE 374

2-(4-Bromo-3-trifluoromethyl-phenylamino)-8-butyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 441, 443 MH^+.

EXAMPLE 375

8-Butyl-2-(3-iodo-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one

MS (CI) 421 MH^+.

EXAMPLE 376

2-(3-Fluoro-4-methyl-phenylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 313 MH^+.

EXAMPLE 377

8-Butyl-2-(3,4-dimethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one

MS (CI) 323 MH^+.

EXAMPLE 378

8-Butyl-2-(1H-indol-5-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one

MS (CI) 334 MH^+.

EXAMPLE 379

8-Butyl-2-(1H-indazol-5-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one

MS (CI) 335 MH^+.

EXAMPLE 380

2-(1H-Benzotriazol-5-ylamino)-8-butyl-8H-pyrido[2,3-d]pyrimidin-7-one

MS (CI) 336 MH^+.

EXAMPLE 381

[4-(8-Butyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-phenyl]-carbamic acid tert-butyl ester MS (CI) 410 MH^+.

EXAMPLE 382

8-Butyl-2-(2-fluoro-4-hydroxy-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 329 MH^+.

EXAMPLE 383

8-Butyl-2-(3-chloro-4-hydroxy-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 345 MH^+.

EXAMPLE 384

8-Butyl-2-(3,5-dichloro-4-hydroxy-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 379 MH^+.

EXAMPLE 385

8-Butyl-2-(4-methoxy-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 325 MH^+.

EXAMPLE 386

8-Butyl-2-(3,4-dimethoxy-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 355 MH^+.

EXAMPLE 387

8-Butyl-2-(4-fluoro-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 313 MH^+.

EXAMPLE 388

8-Butyl-2-(4-chloro-3-methyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 343 MH^+.

EXAMPLE 389

8-Butyl-2-(3,4,5-trimethoxy-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 385 MH^+.

EXAMPLE 390

8-Butyl-2-(4-fluoro-3-trifluoromethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 381 MH^+.

EXAMPLE 391

8-Butyl-2-(3,5-dichloro-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one

MS (CI) 363 MH^+.

EXAMPLE 392

8-Butyl-2-(4-fluoro-3-methyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 327 MH^+.

EXAMPLE 393

4-(8-Butyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-benzenesulfonamide MS (CI) 374 MH^+.

EXAMPLE 394

8-Butyl-2-(3-fluoro-4-methoxy-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 343 MH^+.

EXAMPLE 395

N-[5-(8-Butyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-2-cyano-phenyl]-acetamide MS (CI) 377 MH^+.

EXAMPLE 396

8-Butyl-2-(3-methoxy-5-trifluoromethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 393 MH^+.

EXAMPLE 397

8-Butyl-2-(3,4-difluoro-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 331 MH^+.

EXAMPLE 398

8-Butyl-2-(3-chloro-4-iodo-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 455 MH^+.

EXAMPLE 399

8-Butyl-2-(3,5-dimethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 323 MH^+.

EXAMPLE 400

8-Butyl-2-(3-chloro-4-methyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 343 MH^+.

EXAMPLE 401

8-Butyl-2-(4-chloro-3-trifluoromethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 397 MH^+.

EXAMPLE 402

3-(8-Butyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-benzenesulfonamide MS (CI) 374 MH^+.

EXAMPLE 403

8-Butyl-2-(5-oxo-5,6,7,8-tetrahydro-naphthalen-2-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 363 MH^+.

EXAMPLE 404

8-Butyl-2-(3,5-difluoro-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 331 MH^+.

EXAMPLE 405

N-[5-(8-Butyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-2-methyl-phenyl]-methanesulfonamide MS (CI) 402 MH^+.

EXAMPLE 406

8-Isopropyl-2-(3-nitro-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 326 MH^+.

EXAMPLE 407

2-(4-Fluoro-3-trifluoromethyl-phenylamino)-8-isopropyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 367 MH^+.

EXAMPLE 408

2-(4-Fluoro-3-methyl-phenylamino)-8-isopropyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 313 MH^+.

EXAMPLE 409

2-(1H-Indol-5-ylamino)-8-isopropyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 320 MH^+.

EXAMPLE 410

2-(1H-Benzotriazol-5-ylamino)-8-isopropyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 322 MH^+.

EXAMPLE 411

[4-(8-Isopropyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-phenyl]-carbamic acid tert-butyl ester MS (CI) 396 MH^+.

EXAMPLE 412

2-(3,5-Dichloro-4-hydroxy-phenylamino)-8-isopropyl-8H-pyrido[2,3-d]pyrimidin-7-one

EXAMPLE 413

2-(3-Chloro-4-hydroxy-phenylamino)-8-isopropyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 331 MH^+.

EXAMPLE 414

N-[4-(8-Isopropyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-phenyl]-acetamide MS (CI) 338 MH^+.

EXAMPLE 415

8-Butyl-2-(2-fluoro-5-nitro-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 358 MH^+.

EXAMPLE 416

2-(4-Chloro-3-methyl-phenylamino)-8-isopropyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 332 MH^+.

EXAMPLE 417

8-Isopropyl-2-(3,4,5-trimethoxy-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 371 MH^+.

EXAMPLE 418

4-(8-Isopropyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-benzenesulfonamide MS (CI) 360 MH^+.

EXAMPLE 419

2-(3-Chloro-4-fluoro-phenylamino)-8-isopropyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 333 MH^+.

EXAMPLE 420

2-(2-Fluoro-5-nitro-phenylamino)-8-isopropyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 344 MH^+.

EXAMPLE 421

2-(4-Chloro-3-trifluoromethyl-phenylamino)-8-isopropyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 383 MH^+.

EXAMPLE 422

2-(3-Fluoro-4-methoxy-phenylamino)-8-isopropyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 329 MH^+.

EXAMPLE 423

4-(8-Isopropyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-phthalonitrile MS (CI) 331 MH^+.

EXAMPLE 424

N-[2-Cyano-5-(8-isopropyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-phenyl]-acetamide MS (CI) 363 MH^+.

EXAMPLE 425

8-Isopropyl-2-(3-methoxy-5-trifluoromethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 379 MH^+.

EXAMPLE 426

2-(3,4-Difluoro-phenylamino)-8-isopropyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 317 MH^+.

EXAMPLE 427

2-(3-Iodo-4-methyl-phenylamino)-8-isopropyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 421 MH^+.

EXAMPLE 428

2-(2-Fluoro-5-trifluoromethyl-phenylamino)-8-isopropyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 367 MH^+.

EXAMPLE 429

2-(3,5-Dichloro-phenylamino)-8-isopropyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 349 MH^+.

EXAMPLE 430

3-(8-Isopropyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-benzenesulfonamide MS (CI) 360 MH^+.

EXAMPLE 431

8-Isopropyl-2-(5-oxo-5,6,7,8-tetrahydro-naphthalen-2-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 349 MH^+.

EXAMPLE 432

N-[4-(8-Isopropyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-phenyl]-N-methyl-acetamide MS (CI) 352 MH^+.

EXAMPLE 433

4-(8-Isopropyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-benzonitrile MS (CI) 306 MH^+.

EXAMPLE 434

2-(3,4-Dimethyl-phenylamino)-8-isopropyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 309 MH^+.

EXAMPLE 435

2-(4-Hydroxy-3-methyl-phenylamino)-8-isopropyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 311 MH^+.

EXAMPLE 436

2-(4-Hydroxy-3-morpholin-4-ylmethyl-phenylamino)-8-isopropyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 396 MH^+.

EXAMPLE 437

2-(2,3-Dihydro-1H-indol-5-ylamino)-8-isopropyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 322 MH^+.

EXAMPLE 438

2-(1H-Indazol-6-ylamino)-8-isopropyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 321 MH^+.

EXAMPLE 439

N-[5-(8-Isopropyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-2-methyl-phenyl]-methanesulfonamide MS (CI) 388 MH^+.

EXAMPLE 440

N-[5-(8-Isopropyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-2-methyl-phenyl]-acetamide MS (CI) 352 MH^+.

EXAMPLE 441

2-(4-Hydroxy-3,5-dimethyl-phenylamino)-8-isopropyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 325 MH^+.

EXAMPLE 442

2-(4-Bromo-3-methyl-phenylamino)-8-isopropyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 373 MH^+.

EXAMPLE 443

8-Isopropyl-2-(4-trifluoromethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 349 MH^+.

EXAMPLE 444

8-Isopropyl-2-(4-trifluoromethoxy-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 365 MH^+.

EXAMPLE 445

N-[2-Cyano-4-(8-isopropyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-phenyl]-acetamide MS (CI) 362 MH^+.

EXAMPLE 446

8-sec-Butyl-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 295 MH^+.

EXAMPLE 447

8-sec-Butyl-2-(1H-indol-5-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 334 MH^+.

EXAMPLE 448

8-sec-Butyl-2-(1H-indazol-5-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one

MS (CI) 335 MH^+.

EXAMPLE 449

2-(1H-Benzotriazol-5-ylamino)-8-sec-butyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 336 MH^+.

EXAMPLE 450

[4-(8-sec-Butyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-phenyl]-carbamic acid tert-butyl ester MS (CI) 410 MH^+.

EXAMPLE 451

8-sec-Butyl-2-(2-fluoro-4-hydroxy-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 329 MH^+.

EXAMPLE 452

8-sec-Butyl-2-(3-chloro-4-hydroxy-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 345 MH^+.

EXAMPLE 453

8-sec-Butyl-2-(3-nitro-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 340 MH^+.

EXAMPLE 454

8-sec-Butyl-2-(3,4-dimethoxy-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 355 MH^+.

EXAMPLE 455

8-sec-Butyl-2-(4-methoxy-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 325 MH^+.

EXAMPLE 456

8-sec-Butyl-2-(4-chloro-3-methyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 343 MH^+.

EXAMPLE 457

8-sec-Butyl-2-(3,4,5-trimethoxy-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 385 MH^+.

EXAMPLE 458

8-sec-Butyl-2-(4-fluoro-3-trifluoromethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 381 MH^+.

EXAMPLE 459

8-sec-Butyl-2-(2-fluoro-5-nitro-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 358 MH^+.

EXAMPLE 460

8-sec-Butyl-2-(3-chloro-4-fluoro-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 347 MH^+.

EXAMPLE 461

8-sec-Butyl-2-(3,4,5-trichloro-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 397 MH^+.

EXAMPLE 462

8-sec-Butyl-2-(3-fluoro-4-methoxy-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 343 MH^+.

EXAMPLE 463

8-sec-Butyl-2-(3-methoxy-5-trifluoromethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 393 MH^+.

EXAMPLE 464

8-sec-Butyl-2-(3-chloro-4-iodo-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 455 MH^+.

EXAMPLE 465

8-sec-Butyl-2-(3-iodo-4-methyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 435 MH^+.

EXAMPLE 466

8-sec-Butyl-2-(2-fluoro-5-trifluoromethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 381 MH^+.

EXAMPLE 467

8-sec-Butyl-2-(3-chloro-4-methyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 343 MH^+.

EXAMPLE 468

8-sec-Butyl-2-(4-chloro-3-trifluoromethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 397 MH^+.

EXAMPLE 469

3-(8-sec-Butyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-benzenesulfonamide MS (CI) 374 MH^+.

EXAMPLE 470

8-sec-Butyl-2-(5-oxo-5,6,7,8-tetrahydro-naphthalen-2-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 363 MH^+.

EXAMPLE 471

N-[4-(8-sec-Butyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-phenyl]-N-methyl-acetamide MS (CI) 366 MH^+.

EXAMPLE 472

8-sec-Butyl-2-(3,5-difluoro-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 331 MH^+.

EXAMPLE 473

8-Cyclopentyl-2-(2,4,6-trifluoro-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 363 MH^+.

EXAMPLE 474

4-(8-sec-Butyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-benzonitrile MS (CI) 320 MH^+.

EXAMPLE 475

8-sec-Butyl-2-(4-fluoro-3-nitro-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 358 MH^+.

EXAMPLE 476

8-sec-Butyl-2-(3,4-dimethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 323 MH^+.

EXAMPLE 477

8-sec-Butyl-2-(3-trifluoromethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 363 MH^+.

EXAMPLE 478

2-(3-Bromo-4-methyl-phenylamino)-8-sec-butyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 387 MH^+.

EXAMPLE 479

2-(4-Bromo-3-methyl-phenylamino)-8-sec-butyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 387 MH^+.

EXAMPLE 480

N-[5-(8-sec-Butyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-2-methyl-phenyl]-methanesulfonamide MS (CI) 402 MH^+.

EXAMPLE 481

2-(3-Chloro-4-fluoro-phenylamino)-8-(1-ethyl-propyl)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 361 MH^+.

EXAMPLE 482

8-(1-Ethyl-propyl)-2-(3-fluoro-4-methyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 341 MH^+.

EXAMPLE 483

2-(2,4-Difluoro-phenylamino)-8-(1-ethyl-propyl)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 345 MH^+.

EXAMPLE 484

4-[8-(1-Ethyl-propyl)-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino]-benzonitrile MS (CI) 334 MH^+.

EXAMPLE 485

8-(1-Ethyl-propyl)-2-(3-trifluoromethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 380 MH^+.

EXAMPLE 486

2-(4-Chloro-3-trifluoromethyl-phenylamino)-8-(1-ethyl-propyl)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 411 MH^+.

EXAMPLE 487

8-(1-Ethyl-propyl)-2-(3-trifluoromethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 377 MH^+.

EXAMPLE 488

2-(4-Bromo-3-trifluoromethyl-phenylamino)-8-(1-ethyl-propyl)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 455, 457 MH^+.

EXAMPLE 489

8-(1-Ethyl-propyl)-2-(3-nitro-4-trifluoromethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 421 MH^+.

EXAMPLE 490

8-(1-Ethyl-propyl)-2-(3-iodo-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 435 MH^+.

EXAMPLE 491

2-(3,4-Dimethyl-phenylamino)-8-(1-ethyl-propyl)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 337 MH^+.

EXAMPLE 492

8-(1-Ethyl-propyl)-2-(1H-indol-5-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 348 MH^+.

EXAMPLE 493

8-(1-Ethyl-propyl)-2-(2-oxo-2,3-dihydro-1H-benzimidazol-5-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 365 MH^+.

EXAMPLE 494

{4-[8-(1-Ethyl-propyl)-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino]-phenyl}-carbamic acid tert-butyl ester MS (CI) 424 MH^+.

EXAMPLE 495

8-(1-Ethyl-propyl)-2-(2-fluoro-4-hydroxy-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 343 MH^+.

EXAMPLE 496

2-(3-Chloro-4-hydroxy-phenylamino)-8-(1-ethyl-propyl)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 359 MH^+.

EXAMPLE 497

2-(3,5-Dichloro-4-hydroxy-phenylamino)-8-(1-ethyl-propyl)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 393 MH^+.

EXAMPLE 498

8-(1-Ethyl-propyl)-2-(3-nitro-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 354 MH^+.

EXAMPLE 499

2-(3,4-Dimethoxy-phenylamino)-8-(1-ethyl-propyl)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 369 MH^+.

EXAMPLE 500

2-(4-Chloro-3-methyl-phenylamino)-8-(1-ethyl-propyl)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 357 MH^+.

EXAMPLE 501

8-(1-Ethyl-propyl)-2-(3,4,5-trimethoxy-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 399 MH^+.

EXAMPLE 502

8-(1-Ethyl-propyl)-2-(4-fluoro-3-trifluoromethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 395 MH^+.

EXAMPLE 503

8-(1-Ethyl-propyl)-2-(4-fluoro-3-methyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 341 MH^+.

EXAMPLE 504

8-(1-Ethyl-propyl)-2-(2-fluoro-5-nitro-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 372 MH^+.

EXAMPLE 505

8-(1-Ethyl-propyl)-2-(3-fluoro-4-methoxy-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 357 MH^+.

EXAMPLE 506

N-{2-Cyano-5-[8-(1-ethyl-propyl)-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino]-phenyl}-acetamide MS (CI) 391 MH^+.

EXAMPLE 507

2-(4-Bromo-3-chloro-phenylamino)-8-(1-ethyl-propyl)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 421 MH^+.

EXAMPLE 508

8-(1-Ethyl-propyl)-2-(3-methoxy-5-trifluoromethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 407 MH^+.

EXAMPLE 509

2-(3,4-Difluoro-phenylamino)-8-(1-ethyl-propyl)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 345 MH^+.

EXAMPLE 510

2-(3,5-Difluoro-phenylamino)-8-(1-ethyl-propyl)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 345 MH^+.

EXAMPLE 511

2-(3,4-Dichloro-phenylamino)-8-(1-ethyl-propyl)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 377 MH^+.

EXAMPLE 512

8-(1-Ethyl-propyl)-2-(3-hydroxy-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 325 MH^+.

EXAMPLE 513

N-{4-[8-(1-Ethyl-propyl)-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino]-2-methyl-phenyl}-acetamide MS (CI) 380 MH^+.

EXAMPLE 514

N-{2-Chloro-4-[8-(1-ethyl-propyl)-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino]-6-fluoro-phenyl}-acetamide MS (CI) 418 MH^+.

EXAMPLE 515

8-(1-Ethyl-propyl)-2-(4-trifluoromethoxy-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 393 MH^+.

EXAMPLE 516

2-(9H-Carbazol-3-ylamino)-8-(1-ethyl-propyl)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 398 MH^+.

EXAMPLE 517

8-(1-Ethyl-propyl)-2-(2-oxo-2,3-dihydro-benzoxazol-5-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 366 MH^+.

EXAMPLE 518

8-(1-Ethyl-propyl)-2-(1H-indazol-6-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 349 MH^+.

EXAMPLE 519

N-{5-[8-(1-Ethyl-propyl)-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino]-2-methyl-phenyl}-methanesulfonamide MS (CI) 416 MH^+.

EXAMPLE 520

8-(1-Ethyl-propyl)-2-(3-oxo-3,4-dihydro-2H-1,4-benzothiazin-6-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 396 MH^+.

EXAMPLE 521

2-(4-Amino-3,5-dichloro-phenylamino)-8-(1-ethyl-propyl)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 392 MH^+.

EXAMPLE 522

N-{5-[8-(1-Ethyl-propyl)-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino]-2-methyl-phenyl}-acetamide MS (CI) 380 MH^+.

EXAMPLE 523

8-(1-Ethyl-propyl)-2-(4-hydroxy-3,5-dimethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 353 MH^+.

EXAMPLE 524

5-[8-(1-Ethyl-propyl)-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino]-2-hydroxy-benzoic acid MS (CI) 369 MH^+.

EXAMPLE 525

8-(1-Ethyl-propyl)-2-(indan-5-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 349 MH^+.

EXAMPLE 526

8-(1-Ethyl-propyl)-2-(4-trifluoromethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 377 MH^+.

EXAMPLE 527

2-(4-Bromo-3-methyl-phenylamino)-8-(1-ethyl-propyl)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 401 MH^+.

EXAMPLE 528

8-Cyclopentyl-2-(1H-indol-5-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 346 MH^+.

EXAMPLE 529

8-Cyclopentyl-2-(1H-indazol-6-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one

MS (CI) 347 MH^+.

EXAMPLE 530

8-Cyclopentyl-2-(3-trifluoromethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 375 MH^+.

EXAMPLE 531

4-(8-Cyclopentyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-benzonitrile MS (CI) 332 MH^+.

EXAMPLE 532

8-Cyclopentyl-2-(3,4-dichloro-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 375 MH^+.

EXAMPLE 533

8-Cyclopentyl-2-(4-trifluoromethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 375 MH^+.

EXAMPLE 534

8-Cyclopentyl-2-(4-fluoro-3-trifluoromethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 393 MH^+.

EXAMPLE 535

[4-(8-Cyclopentyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-phenyl]-carbamic acid tert-butyl ester MS (CI) 422 MH^+.

EXAMPLE 536

8-Cyclopentyl-2-(1H-indazol-5-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 347 MH^+.

EXAMPLE 537

2-(1H-Benzotriazol-5-ylamino)-8-cyclopentyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 348 MH^+.

EXAMPLE 538

8-Cyclopentyl-2-(2-fluoro-4-hydroxy-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 341 MH^+.

EXAMPLE 539

2-(3-Chloro-4-hydroxy-phenylamino)-8-cyclopentyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 357 MH^+.

EXAMPLE 540

8-Cyclopentyl-2-(3,5-dichloro-4-hydroxy-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 391 MH^+.

EXAMPLE 541

8-Cyclopentyl-2-(3,4-dimethoxy-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 367 MH^+.

EXAMPLE 542

8-Cyclopentyl-2-(3-fluoro-4-methoxy-phenylamino)-8H-pyido[2,3-d]pyrimidin-7-one MS (CI) 341 MH^+.

EXAMPLE 543

8-Cyclopentyl-2-(3-methoxy-5-trifluoromethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 405 MH^+.

EXAMPLE 544

8-Cyclopentyl-2-(3,5-dimethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 335 MH^+.

EXAMPLE 545

2-(3-Chloro-4-methyl-phenylamino)-8-cyclopentyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 355 MH^+.

EXAMPLE 546

2-(4-Chloro-3-trifluoromethyl-phenylamino)-8-cyclopentyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 409 MH^+.

EXAMPLE 547

3-(8-Cyclopentyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-benzenesulfonamide MS (CI) 386 MH^+.

EXAMPLE 548

8-Cyclopentyl-2-(3,5-difluoro-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 343 MH^+.

EXAMPLE 549

8-Cyclopentyl-2-(3,4-dimethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 335 MH^+.

EXAMPLE 550

8-Cyclopentyl-2-(4-hydroxy-3-morpholin-4-ylmethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 422 MH^+.

EXAMPLE 551

8-Cyclopentyl-2-(4-hydroxy-3-nitro-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 368 MH^+.

EXAMPLE 552

8-Cyclopentyl-2-(2,3-dimethyl-2,3-dihydro-1H-indol-5-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 375 MH^+.

EXAMPLE 553

8-Cyclopentyl-2-(2,3-dihydro-1H-indol-5-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 348 MH^+.

EXAMPLE 554

8-Cyclopentyl-2-(2-oxo-2,3-dihydro-benzoxazol-5-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 364 MH^+.

EXAMPLE 555

N-[5-(8-Cyclopentyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-2-methyl-phenyl]-methanesulfonamide MS (CI) 414 MH^+.

EXAMPLE 556

8-Cyclopentyl-2-(3-oxo-3,4-dihydro-2H-1,4-benzothiazin-6-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 394 MH^+.

EXAMPLE 557

2-(4-Amino-3,5-dichloro-phenylamino)-8-cyclopentyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 390 MH^+.

EXAMPLE 558

N-[5-(8-Cyclopentyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-2-methyl-phenyl]-acetamide MS (CI) 378 MH^+.

EXAMPLE 559

8-Cyclopentyl-2-(4-hydroxy-3,5-dimethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 351 MH^+.

EXAMPLE 560

5-(8-Cyclopentyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-2-hydroxy-benzoic acid MS (CI) 367 MH^+.

EXAMPLE 561

2-(4-Bromo-3-trifluoromethyl-phenylamino)-8-cyclopentyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 361 MH^+.

EXAMPLE 562

2-(4-Bromo-3-methyl-phenylamino)-8-cyclopentyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 399 MH^+.

EXAMPLE 563

8-Cyclopropylmethyl-2-(1H-indol-5-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 332 MH^+.

EXAMPLE 564

2-(1H-Benzotriazol-5-ylamino)-8-cyclopropylmethyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 334 MH^+.

EXAMPLE 565

[4-(8-Cyclopropylmethyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-phenyl]-carbamic acid tert-butyl ester MS (CI) 408 MH^+.

EXAMPLE 566

8-Cyclopropylmethyl-2-(2-fluoro-4-hydroxy-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 327 MH^+.

EXAMPLE 567

2-(3-Chloro-4-hydroxy-phenylamino)-8-cyclopropylmethyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 343 MH^+.

EXAMPLE 568

8-Cyclopropylmethyl-2-(3,5-dichloro-4-hydroxy-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 377 MH^+.

EXAMPLE 569

8-Cyclopropylmethyl-2-(3,4,5-trimethoxy-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 383 MH^+.

EXAMPLE 570

8-Cyclopropylmethyl-2-(4-fluoro-3-trifluoromethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 379 MH^+.

EXAMPLE 571

4-(8-Cyclopropylmethyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-benzenesulfonamide MS (CI) 372 MH^+.

EXAMPLE 572

8-Cyclopropylmethyl-2-(2-fluoro-5-nitro-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 356 MH^+.

EXAMPLE 573

2-(3-Chloro-4-iodo-phenylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 352 MH^+.

EXAMPLE 574

N-[2-Cyano-5-(8-cyclopropylmethyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-phenyl]-acetamide MS (CI) 375 MH^+.

EXAMPLE 575

8-Cyclopropylmethyl-2-(3,5-difluoro-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 329 MH^+.

EXAMPLE 576

8-Cyclopropylmethyl-2-(4-fluoro-3-nitro-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 356 MH^+.

EXAMPLE 577

8-Cyclopropylmethyl-2-(2-oxo-2,3-dihydro-1H-benzimidazol-5-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 349 MH^+.

EXAMPLE 578

8-Cyclopropylmethyl-2-(3-hydroxy-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one 308.3394, 309. MS (CI) 309 MH^+.

EXAMPLE 579

N-[2-Chloro-4-(8-cyclopropylmethyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-6-fluoro-phenyl]-acetamide 401.8273, 402. MS (CI) 402 MH^+.

EXAMPLE 580

8-Cyclopropylmethyl-2-(2,3-dimethyl-2,3-dihydro-1H-indol-5-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 361 MH^+.

EXAMPLE 581

8-Cyclopropylmethyl-2-(2,3-dihydro-1H-indol-5-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 334 MH^+.

EXAMPLE 582

2-(9H-Carbazol-3-ylamino)-8-cyclopropylmethyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 382 MH^+.

EXAMPLE 583

8-Cyclopropylmethyl-2-(1H-indazol-6-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 570 MH^+.

EXAMPLE 584

8-Cyclopropylmethyl-2-(3-oxo-3,4-dihydro-2H-1,4-benzothiazin-6-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 380 MH^+.

EXAMPLE 585

N-[5-(8-Cyclopropylmethyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-2-methyl-phenyl]-acetamide MS (CI) 364 MH^+.

EXAMPLE 586

8-Cyclopropylmethyl-2-(4-hydroxy-3,5-dimethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 337 MH^+.

EXAMPLE 587

8-Cyclopropylmethyl-2-(indan-5-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 333 MH^+.

EXAMPLE 588

8-Cyclopropylmethyl-2-(3,4,5-trifluoro-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 347 MH^+.

EXAMPLE 589

2-(4-Bromo-3-trifluoromethyl-phenylamino)-8-cyclopropylmethyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 441 MH^+.

EXAMPLE 590

8-Cyclopropylmethyl-2-(4-trifluoromethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 361 MH^+.

EXAMPLE 591

8-Cyclopropylmethyl-2-(4-trifluoromethoxy-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 377 MH^+.

EXAMPLE 592

N-[5-(8-Cyclopropylmethyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-2-methyl-phenyl]-methanesulfonamide MS (CI) 400 MH^+.

EXAMPLE 593

2-(1H-Indol-5-ylamino)-8-(2,2,2-trifluoro-ethyl)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 360 MH^+.

EXAMPLE 594

2-(1H-Indazol-5-ylamino)-8-(2,2,2-trifluoro-ethyl)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 361 MH^+.

EXAMPLE 595

2-(1H-Benzotriazol-5-ylamino)-8-(2,2,2-trifluoro-ethyl)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 362 MH^+.

EXAMPLE 596

2-(2-Fluoro-4-hydroxy-phenylamino)-8-(2,2,2-trifluoro-ethyl)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 355 MH^+.

EXAMPLE 597

2-(3-Chloro-4-hydroxy-phenylamino)-8-(2,2,2-trifluoro-ethyl)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 371 MH^+.

EXAMPLE 598

2-(3,5-Dichloro-4-hydroxy-phenylamino)-8-(2,2,2-trifluoro-ethyl)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 405 MH^+.

EXAMPLE 599

2-(3-Nitro-phenylamino)-8-(2,2,2-trifluoro-ethyl)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 366 MH^+.

EXAMPLE 600

2-(3,4-Dimethoxy-phenylamino)-8-(2,2,2-trifluoro-ethyl)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 381 MH^+.

EXAMPLE 601

2-Phenylamino-8-(2,2,2-trifluoro-ethyl)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 321 MH^+.

EXAMPLE 602

2-(3-Fluoro-4-methoxy-phenylamino)-8-(2,2,2-trifluoro-ethyl)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 369 MH^+.

EXAMPLE 603

4-[7-Oxo-8-(2,2,2-trifluoro-ethyl)-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino]-phthalonitrile MS (CI) 371 MH^+.

EXAMPLE 604

N-{2-Cyano-5-[7-oxo-8-(2,2,2-trifluoro-ethyl)-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino]-phenyl}-acetamide MS (CI) 403 MH^+.

EXAMPLE 605

2-(4-Bromo-3-chloro-phenylamino)-8-(2,2,2-trifluoro-ethyl)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 433 MH^+.

EXAMPLE 606

2-(3-Methoxy-5-trifluoromethyl-phenylamino)-8-(2,2,2-trifluoro-ethyl)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 419 MH^+.

EXAMPLE 607

2-(3,4-Difluoro-phenylamino)-8-(2,2,2-trifluoro-ethyl)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 357 MH^+.

EXAMPLE 608

8-(2,2,2-Trifluoro-ethyl)-2-(2,4,6-trifluoro-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 375 MH^+.

EXAMPLE 609

2-(3,5-Difluoro-phenylamino)-8-(2,2,2-trifluoro-ethyl)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 357 MH^+.

EXAMPLE 610

2-(4-Fluoro-3-nitro-phenylamino)-8-(2,2,2-trifluoro-ethyl)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 384 MH^+.

EXAMPLE 611

8-(2,2,2-Trifluoro-ethyl)-2-(3-trifluoromethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 389 MH^+.

EXAMPLE 612

N-{2-Methyl-4-[7-oxo-8-(2,2,2-trifluoro-ethyl)-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino]-phenyl}-acetamide MS (CI) 392 MH^+.

EXAMPLE 613

8-Cyclohexyl-2-(3,4-dimethoxy-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 381 MH^+.

EXAMPLE 614

2-(1H-Indol-5-ylamino)-8-methyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 292 MH^+.

EXAMPLE 615

[4-(8-Methyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-phenyl]-carbamic acid tert-butyl ester MS (CI) 368 MH^+.

EXAMPLE 616

2-(3-Chloro-4-hydroxy-phenylamino)-8-methyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 303 MH^+.

EXAMPLE 617

2-(3,4-Dimethoxy-phenylamino)-8-methyl-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 313 MH^+.

EXAMPLE 618

2-(2-Fluoro-5-nitro-phenylamino)-8-methyl-8H-pyrido[2,3-d]pyrimidin-7-one

MS (CI) 316 MH^+.

EXAMPLE 619

8-Methyl-2-(3,4,5-trimethoxy-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 343 MH^+.

EXAMPLE 620

4-(8-Methyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-2-trifluoromethyl-benzonitrile MS (CI) 346 MH^+.

EXAMPLE 621

8-Ethyl-2-(1H-indol-5-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one MS (CI) 306 MH^+.

EXAMPLE 622

8-Isopropyl-2-(4-methoxy-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one

2-Chloro-8-isopropyl-8*H*-pyrido[2,3-*d*]pyrimidin-7-one (100 mg, 0.42 mmol) and 4-methoxy-phenylamine (80 mg, 0.5 mmol) were mixed together and fused at 300°C. The crude mass was then broken up in 1 mL of $CHCl_3$ and purified by chromatography (silica gel, 30% ethyl acetate in hexane). The purified material was then crystallized from ethyl acetate to give the title compound (89 mg, 68%) as a gray powder, mp 170°C.

Analysis calc'd for $C_{17}H_{18}N_4O_2$ 0.16 H_2O: C, 65.19; H, 5.90; N, 17.89. Found: C, 64.82; H, 5.80; N, 17.78.

EXAMPLE 623

8-Isopropyl-2-(3-nitro-phenylamino)-8*H*-pyrido[2,3-*d*]pyrimidin-7-one

2-Chloro-8-isopropyl-8*H*-pyrido[2,3-*d*]pyrimidin-7-one (100 mg, 0.42 mmol) and 3-nitro-phenylamine (70 mg, 0.5 mmol) were mixed together and fused at 300°C. The crude mass was then broken up in 1 mL of $CHCl_3$ and purified by chromatography (silica gel, 30% ethyl acetate in hexane). The purified material was then crystallized from ethyl acetate to give the title compound (90 mg, 66%) as a bright yellow powder, mp 202-203°C.

Analysis calculated for $C_{16}H_{15}N_5O_3$: C, 58.77; H, 4.43; N, 21.24.
Found: C, 59.07; H, 4.65; N, 21.53.

EXAMPLE 624

8-Isopropyl-2-(4-hydroxy-phenylamino)-8*H*-pyrido[2,3-*d*]pyrimidin-7-one

2-Chloro-8-isopropyl-8*H*-pyrido[2,3-*d*]pyrimidin-7-one (50 mg, 0.22 mmol) and 4-amino-phenol (36 mg, 0.33 mmol) were mixed together and fused at 300°C. The crude mass was then broken up in 1 mL of $CHCl_3$ and purified by chromatography (silica gel, 30% ethyl acetate in hexane). The purified material was then crystallized from ethyl acetate to give the title compound (52 mg, 80%) as a yellow powder, mp >220°C.
Analysis calculated for $C_{16}H_{16}N_4O_2$: C, 64.85; H, 5.44; N, 18.91.
Found: C, 64.68; H, 5.37; N, 18.77.

As noted above, the compounds of this invention are potent inhibitors of cyclin-dependent kinases, and accordingly, are useful in treating and preventing neurodegenerative diseases such as Alzheimer's disease and Huntington's disease. The compounds have exhibited excellent inhibitory activity against a wide variety of cyclin-dependent kinases, all in assay systems routinely utilized to measure such activity. A typical assay, for instance, measures inhibitory activity against the cyclin D dependent kinase 4 enzyme (cdk4/D). The invention compounds of Formulas I and II exhibited IC_{50} values ranging generally from 0.0045 μM to 10 μM. The cdk4 assay was carried out as follows.

Cyclin-Dependent Kinase 4 (cdk4) Assay

Enzyme assays for IC_{50} determinations (Tables 1 and 2) and kinetic evaluation were performed in 96-well filter plates (Millipore MADVN6550). The total volume was 0.1 mL containing a final concentration of 20 mM TRIS (tris[hydroxymethyl]aminomethane), at pH 7.4, 50 mM NaCl, 1 mM dithiothreitol, 10 mM $MgCl_2$, 25 μM ATP containing 0.25 μCi of [^{32}P]ATP, 20 ng of cdk4, 1 μg of retinoblastoma, and appropriate dilutions of a compound of the present invention. All components except the ATP were added to the wells,

and the plate was placed on a plate mixer for 2 minutes. The reaction was started by adding [^{32}P]ATP and the plate was incubated at 25°C for 15 minutes. The reaction was terminated by addition of 0.1 mL of 20% trichloroacetic acid (TCA). The plate was kept at 4°C for at least 1 hour to allow the substrate to precipitate. The wells were then washed five times with 0.2 mL of 10% TCA and ^{32}P incorporation was determined with a beta plate counter (Wallac Inc., Gaithersburg, MD).

Cyclin-Dependent Kinase Assays (cdk2/cyclinE, cdk2/cyclinA, cdc2/cyclinB)

Enzyme assays for IC_{50} determinations and kinetic evaluation were performed in a 96-well filter plate (Millipore MADVN6550) in a total volume of 0.1 mL of 20 mM TRIS (tris[hydroxymethyl]aminomethane), at pH 7.4, 50 mM NaCl, 1 mM dithiothreitol, 10 mM $MgCl_2$, 12 mM ATP containing 0.25 μCi of [^{32}P]ATP, 20 ng of enzyme (either cdk2/cyclinE, cdk2/A, or cdc2/cyclinB), 1 μg retinoblastoma, and appropriate dilutions of the particular invention compound. All components except the ATP were added to the wells, and the plate was placed on a plate mixer for 2 minutes. The reaction was begun by addition of [^{32}P]ATP, and the plate was incubated at 25°C for 15 minutes. The reaction was terminated by addition of 0.1 mL of 20% TCA. The plate was kept at 4°C for at least 1 hour to allow the substrate to precipitate. The wells were then washed five times with 0.2 mL of 10% TCA and ^{32}P incorporation determined with a beta plate counter (Wallac Inc., Gaithersburg, MD).

When measured against cdk2/E, the invention compounds exhibited IC_{50} values ranging generally from about 0.02 to about 25 μM. Against cdk2/A, the compounds exhibited IC_{50} values ranging from about 0.01 to about 14 μM, and against cdk2/B, generally from about 0.06 to about 40 μM. The assays were carried out as described above, and specific data is given in Table 1.

In a preferred embodiment of this invention, neurodegenerative diseases are treated by administering a compound that inhibits cdk5 at therapeutic doses. Compounds that are cdk5 inhibitors can be identified by carrying out the following general assay.

Cyclin-Dependent Kinase 5 (cdk5) Assay

Enzyme assays for IC_{50} determinations and kinetic evaluation were performed in 96-well filter plates (Millipore MAPH NOB10). The total volume was 0.065 mL containing a final concentration of 50 mM TRIS (tris[hydroxymethyl]aminomethane) at pH 7.4, 10 mM NaCl, 10 mM $MgCl_2$, 1 mM dithiothreitol, 11.5 μM ATP containing 0.75 μCi of [^{32}P]ATP, 50 ng Cdk5/p25, 2.88 μg histone, and appropriate dilutions of a compound of the present invention. All components except histone and ATP were added to wells, and the plate was placed on a shaker for 5 minutes. The reaction was started by adding histone and [^{32}P]ATP, and the plate was shaken at 30°C for 45 minutes. The reaction was terminated by addition of 0.1 mL of 150 mM phosphoric acid. The plate was kept at 4°C for 30 minutes to allow substrate to precipitate. The wells were then washed three times with 0.2 mL of 75 mM phosphoric acid and ^{32}P incorporation was determined with a beta plate counter (Wallac Inc, Gaithersburg, MD).

When measured against cdk5 the invention compounds exhibited IC_{50} values ranging generally from about 0.02 to about 25 μM. The assay was carried out as described above and specific data is given in Tables 1 and 3.

Cyclin-Dependent Kinase 5 High Throughput Screening (cdk5-HTS) Assay

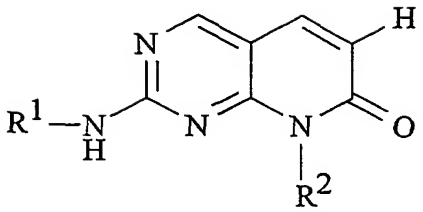
Enzyme assays for IC_{50} determinations were performed in 96-Pierce Reacti-Bind™ White Opaque Glutatione Coated Plates (Cat. No. 15240B).

The total volume was 0.100 mL containing a final concentration of 50 mM TRIS (tris[hydroxymethyl]aminomethane) at pH 7.4, 50 mM NaCl, 10 mM $MgCl_2$, 5 mM dithiothreitol, 20 μM ATP containing 16 μCi/mL of Redivue[γ33P]ATP (Amersham Pharmacia Biotech Cat. No. AH9968), 1.0 μg/mL Cdk5/p25, 20 μg/mL GST-RbCOOH, and appropriate dilutions of a compound of the present invention. The reaction was started by adding [^{33}P]ATP, and the plate was shaken for 30 seconds, then incubated at room temperature for 30 minutes. The reaction was terminated by addition of 0.05 mL of 120 mM EDTA. The plate was kept at room temperature for 45 minutes to allow substrate to bind to the

walls of the plate. The wells were then washed three times with 0.2 mL of 1 × PBS. Once thoroughly dry, 0.140 mL of MicroScint™20 (Packard Bioscience Cat. No. 87-9081) cocktail was added to all wells. The incorporation of ^{33}P was determined with a beta plate counter (Packard Topcount).

When measured against cdk5 in this high throughput screen, the invention compounds exhibited IC_{50} values ranging generally from about 0.02 to about 25 μM. The assay was carried out as described above and specific data is given in Table 4.

Table 1



Example	R^1	R^2	cdk4/D	cdk2/E	cdk2/A	cdk1/B	cdk5
					IC_{50} μM		
18	Ph	Et	0.752	0.41	0.129	1.015	0.065
32	Ph	H	--	12.83	4.66	32.6	1.43
35	Ph	CH_2Ph	0.94	33.85			0.31
36	Ph	CH_2COOMe	31				
37	Ph	CH_2OMe	4.2				
38	Ph	$(CH_2)_3$-OCH_2Ph	2.695	1.75	13.54	29.8	
39	Ph	CH_2-epoxide	5.0				
40	Ph	n-Bu	1.495	0.058	0.037	0.205	
41	Ph	n-Pr	0.55	0.112	0.05	0.299	
42	Ph	CH_2CHMe_2	0.40				0.015
43	Ph	$CHMe_2$	0.15	0.126	0.031	0.44	
44	CH_2Ph	Et			6.46	16.65	
45	Et	Et	12	3.93	2.46	9.23	
46	t-Bu	Et	5.3			3.41	
47	i-Pr	Et	3.7			3.55	
48	cyclohex	Et	3.3	0.592	0.23	2.61	
49	Ph-4-Ph	Et	2.0				
50	4-pyr	Et	2.0				0.027
51	Ph-4-OMe	Et	0.60	0.422	0.134	0.665	0.049
52	Ph-4-$O(CH_2)_2NEt_2$	Et	0.16	2.34	0.75	2.66	0.155
53	Ph-4-pip-4-Me	Et	0.085	1.19	0.339	1.88	0.239
54	Ph-3-OCF_2CF_2H	Et	7.83	1.2	0.238	0.091	0.568
55	Ph-4-OH	Et	0.6				
56	Ph-4-OCH_2Ph	Et	25				
57	Ph-4-$O(CH_2)_2OMe$	Et	0.8				0.218
58	Ph	CH_2Ph-4-OMe	10				

Table 1 (cont'd)

Example	R^1	R^2	cdk4/D	cdk2/E	cdk2/A	cdk1/B	cdk5
					IC_{50} μM		
59	Ph-4-$O(CH_2)_2NEt_2$	$CHMe_2$	0.045	0.8	0.08	1.24	
60	Ph-4-pip-4-Me	$CHMe_2$	0.032	0.27	0.058	0.675	0.017
61	Ph	Me	6.9	0.86	0.49	1.76	
63	CH_2Ph	Me			38.12	21.6	
64	n-Bu	Me	40				
66	$(CH_2)_2$-2-pyridine	Me	45				
67	i-Pr	Me	25				
69[a]	Ph	Et	4.3				0.065
74	Ph	$CHEt_2$	0.141				
77	Ph-4-pip-4-Me	$CHEt_2$	0.014	0.068	0.028	0.141	
78	Ph-4-Net_2	Et	1.3	2.94	2.24	0.74	
79	Ph-4-morpholine	Et	0.3				0.107
83	NHPh	Et (6-Me)	1.8				0.587
84	Ph-4-pip-4-Me	Et (6-Me)	0.18				0.765
85	Ph	CHMeEt	0.2				
86	Ph	CH_2CH_2O-Me	2.4				
87	Ph	$(CH_2)_3OCH_2$-Ph			5.9	1.08	
88	Ph-4-F	Et	1.3	0.28	0.44	2.07	0.053
89	Ph-3-F	Et	1.4				0.393
90	Ph-3-F-4-OMe	Et	1.0				0.029
91	Ph-3-F-2-OMe	Et	9.0				4.45
92	Ph-2-OCH_3	Et					1.68
93	Ph-4-NMe_2	Et	0.38	1.77	0.28	0.78	0.064
100	Et	Ph	19.05				
101	Ph	Ph	1.7				0.165
108	Ph	Cyclopentyl	0.21	0.11	0.012	0.19	0.026
117	Ph-4-$OCH_2CH_2NEt_2$	Cyclopentyl	0.0066	0.109	0.0425		0.019
118	Ph-4-$OCH_2CH_2NEt_2$	Ph	0.200	1.3015	0.2057		0.237
131	Ph	Cyclohexyl	0.047	0.125	0.079	0.749	0.015

Table 1 (cont'd)

Example	R^1	R^2	cdk4/D	cdk2/E	cdk2/A	cdk1/B	cdk5
					IC_{50} μM		
132	Ph-4-$OCH_2CH_2NEt_2$	cyclohexyl	0.0105	0.091	0.0605	0.373	0.0259
133	Ph-4-pip-4-CH_3	cyclohexyl	0.0045	0.0197	0.015	0.0785	0.0069
134	Ph-4-$OCH_2CH_2NEt_2$	cyclopropyl	0.053				0.326
135	Ph	cyclopropyl					0.493
136	Ph-4-pip-4-CH_3	cyclopropyl	0.140				0.24
138	Ph-4-NMe_2	$(CH_2)_3OCH_2Ph$	0.5133	2.63	0.2165	3.295	0.28
139	Ph-4-$O(CH_2)_2NEt_2$	$(CH_2)_2OCH_2Ph$	2.865	2.63			
140	Ph-4-pip-4-CH_3	$(CH_2)_2OCH_2Ph$	2.1	23.6	13.45		5.17
144	Ph-4-pip-3,5-diMe-4-$(CH_2)_2OH$	cyclohexyl	0.016	0.043	0.102	0.344	0.0394
145	Ph-4-pip-3,5-diMe	cyclohexyl	0.0045	0.0455	0.0325	0.1455	0.0173
147	Ph-4-NMe_2	cyclohexyl	0.48	0.081	0.012	0.089	0.024
148	Ph-4-F	cyclohexyl	0.1967	0.0535	0.0775	1.825	
155	Ph	cycloheptyl	0.182	0.024	0.009	0.065	
158	Ph-4-(piperidinyl-1-yl)	3-tetrahydrofuranyl	0.2193	1.9	0.2845	4.34	0.183
159	Ph-4-pip-4-CH_3	cyclohexyl	0.0045	0.0197	0.015	0.0785	0.0069
160	Ph-4-(pyrrolidin-1-yl)	cyclohexyl	0.175		0.061	0.25	0.113
161	Ph-4-(pyrrole-1-yl)	cyclohexyl	0.275	0.554	0.104	0.45	0.0431
162	Ph-4-(pyrazol-1-yl)	cyclohexyl	0.089	0.087	0.0357	0.267	0.0425
163	Ph-4-(piperidinyl-1-yl)	cyclohexyl	0.0315	0.193	0.0668	0.6417	0.15
167	Ph-4-(3,5-dimethylpiperidinyl-1-yl)	cyclohexyl	0.43		0.272	8.915	2.68
171	Ph-4-(3,4-dihydro-1H-isoquinolin-2-yl)	cyclohexyl		0.32	0.1233	1.215	0.419
175	Ph-4-(3-methylpiperidin-1-yl)	cyclohexyl	0.27	0.433	0.7105		0.69

Table 1 (cont'd)

Example	R^1	R^2	cdk4/D	cdk2/E	cdk2/A	cdk1/B	cdk5
					IC_{50} μM		
180	Ph	norbornane	0.038	0.173	0.075	0.503	
181	Ph-4-(piperidinyl-1-yl)	8-bicyclo[2.2.1]-heptyl	0.0577		0.195	33.4	0.591
190	Ph-4-(pyrrol-1-yl)	cyclopentyl	0.1365	0.12			0.0312
191	Ph-4-(pyrazol-1-yl)	cyclohexyl	0.089	0.087	0.0357	0.267	0.0425
195	Ph-4-(3,5-dimethylpyrazol-1-yl)	cyclopentyl	0.133				0.156
196	Ph-4-([4-(2-hydroxyethyl)-piperidin-1-yl)	cyclopentyl	0.017	0.047			0.124
197	Ph-4-([4-(3-hydroxypropyl)-piperidin-1-yl)	cyclopentyl	0.0335	2.3185		7.395	0.1268
198	Ph-4-(4-hydroxypiperidin-1-yl)	cyclopentyl	0.015	0.044		0.118	0.019
200	Ph-4-(piperidin-1-yl)	tetrahydrofuryl	0.219	1.9	0.285	4.34	
202	Ph-3-(piperidinyl-1-yl)	cyclopentyl	0.655				0.0779
203	Ph-3-(piperidinyl-1-yl)	cyclohexyl	0.5				0.0826
206	Ph-4-(4-hydroxypiperidin-1-yl)	cyclopentyl	0.015	0.044		0.118	0.019
206	Ph-4-(3-hydroxymethyl-piperidin-1-yl)	cyclopentyl	0.023				0.0357
211	Ph-4-(piperidin-1-yl)	4-tetrahydropyranyl	0.153	7.6	0.5804		0.3360
212	Ph-4-F	8-bicyclo[2.2.1]-heptyl	0.0297	0.014	0.016	0.1895	0.0101
213	Ph-4-OCF_2CF_3	8-bicyclo[2.2.1]-heptyl	0.3882	10.0	0.275	0.533	0.216
214	Ph-4-(4-(3-hydroxypropyl)-piperidin-1-yl)	8-bicyclo[2.2.1]-heptyl	0.008	0.126	0.205		3.325

Table 1 (cont'd)

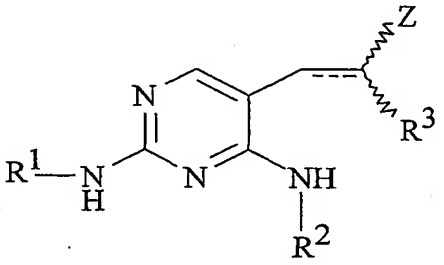
Example	R^1	R^2	cdk4/D	cdk2/E	cdk2/A	cdk1/B	cdk5
					IC_{50} μM		
215	Ph-4-(4-hydroxypiperidin-1-yl)	cyclohexyl	0.0075	0.024	0.0084	0.1122	0.0244
215	Ph-4-(4-(2-hydroxyethyl)-piperidin-1-yl)	cyclohexyl	0.0085	0.03	0.0142	0.1362	0.0329
219	Ph-4-OCF_2CF_3	8-bicyclo[2.2.1]-heptyl	0.78	31.9027	6.6143	7.075	0.5685
220	Ph-3,4-diF	8-bicyclo[2.2.1]-heptyl	0.115	0.05	0.0578	1.66	0.0662
221	Ph-4-SCF_3	8-bicyclo[2.2.1]-heptyl	0.32	0.511	0.37	1.121	0.3490
223	Ph-4-Ph	8-bicyclo[2.2.1]-heptyl		1.95	18.0		0.5870
224	Ph-4-$O(CH_2)_2NEt_2$	8-bicyclo[2.2.1]-heptyl	0.45	0.075	0.0815	0.2	0.0532
227	Ph-4-(4-hydroxypiperidin-1-yl)	8-bicyclo[2.2.1]-heptyl	0.0028	0.056	0.0207	0.0825	0.0360
228	Ph-4-((2-hydroxyethyl)-piperidin-1-yl)	8-bicyclo[2.2.1]-heptyl	0.0055	0.185	0.0985	0.38	0.0388
229	Ph-4-(piperidin-1-yl)	8-bicyclo[2.2.1]-heptyl	2.80	3.0	0.9965	0.44	0.288
231	Ph-4-(3-hydroxymethyl-piperidin-1-yl)	8-bicyclo[2.2.1]-heptyl	0.0021	0.085	0.063	0.22	0.167
235	Ph-4-(3-morpholin-4-yl-propyl)-piperidin-1-yl)	8-bicyclo[2.2.1]-heptyl	0.037		0.096	1.7	1.46
236	Ph-4-(3-(3-hydroxypropyl)-piperidin-1-yl)	8-bicyclo[2.2.1]-heptyl	0.0069		0.0136	0.674	0.3953
237	Ph-4-$OCH_2CH(OH)CH_2NEt_2$	cyclohexyl					
252	Ph-4-pip-Me	8-bicyclo[2.2.1]-heptyl	0.0061	0.102	0.0425	0.16	0.0237
253	Ph-4-(1-hydroxymethyl-piperidin-1-yl)	8-bicyclo[2.2.1]-heptyl	0.0115	0.149	0.11	0.67	0.3
254	Ph-4-(3-hydroxypiperidin-1-yl)	8-bicyclo[2.2.1]-heptyl	0.0035	0.064	0.028	0.175	0.0449

Table 1 (cont'd)

Example	R^1	R^2	cdk4/D	cdk2/E	cdk2/A	cdk1/B	cdk5
					IC_{50} μM		
255	Ph-4-pip-3,5-diMe	8-bicyclo[2.2.1]-heptyl	0.003	0.124	0.0675	0.335	0.0321
258	Ph-4-(2-morpholin-4-yl-ethyl)-piperidin-1-yl	cyclohexyl	0.0075	0.2	0.0733	0.599	

[a] Single bond between C^5 and C^6

Table 2



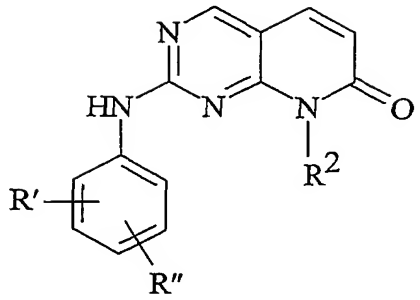
Example	R_1	R_2	R_3	Bond	Z	cdk4/IC_{50} IC_{50} μM	cdk4/D % inhibition at 40 μM
17	Ph	Et	H	trans double	COOEt	2	
68	Ph	Et	H	single	COOEt	90	37%
28	Ph	H	H	trans double	COOEt	65	
73	Ph	Et	Me	trans double	COOEt		58%
72	Ph	Et	H	trans double	CN		18%

Several of the invention compounds have also shown good inhibitory activity against cdk6/D_2 and cdk6/D_3 enzymes. These assays are carried out in a manner similar to that described above for cdk4, by simply employing the appropriate cdk6 kinase enzyme. Invention compounds have shown IC_{50} values ranging from about 0.009 μM to about 0.2 μM. The compound of Example 214,

for instance, had an IC_{50} of 0.0071 μM against cdk6/D_2, and an IC_{50} of 0.013 μM against cdk6/D_3.

As noted above, the cdk inhibitors to be administered according to this invention will have cdk5 inhibitory activity, and preferably will be selectivity more active against cdk5 than against any of the other cdk enzymes. Several of the compounds described above have been tested against a battery of kinase enzymes, and have demonstrated excellent selectivity for cdk5. Tables 3 and 4 show the selectivity of preferred compounds to be used in this invention.

Table 3



				IC_{50}/nM			
Example	R′	R″	R^2	Cdk2/A	Cdk2/E	Cdk4	Cdk5
624	4-OH	H	i-Pr	61	221	255	15
623	3-NO_2	H	i-Pr	297	760	6250	21
622	3-CH_3O	4-CH_3O	Et	392	540	4083	30
111	H	4-CH_3O	i-Pr	120	580	617	9.8
88	4-F	H	Et	421	560	1238	32
61	H	H	CH_3	1150	1680	5480	89
	H	H	1-ethylpropyl	127	200	159	8.7

Table 4

Example	cdk4/D	cdk2/E	cdk2/A	cdk1/B	cdk5-HTS
	IC_{50} μM	IC_{50} μM	IC_{50} μM	IC_{50} μM	IC_{50} μM
285	2.7500	2.2667	2.8000	0.8650	0.2550
286	0.4750	0.2233	0.6300	0.2750	0.1085
287	0.8100	0.1467	0.3650	0.3500	0.0810
288	0.9650	1.0600	1.2500	0.4850	0.2950
289	3.2500	1.1650	2.0000	1.2500	0.7200
290	1.6900	0.1833	0.4300	0.1650	0.2440
291	2.0500	0.4433	0.7900	0.4400	0.4450
292		1.2000		0.8600	0.6100
293	2.0000	0.2500	1.5000	0.4300	0.0400
294	0.4100	0.1300	0.6400	0.2100	0.0430

Table 4 (cont'd)

Example	cdk4/D IC_{50} μM	cdk2/E IC_{50} μM	cdk2/A IC_{50} μM	cdk1/B IC_{50} μM	cdk5-HTS IC_{50} μM
295	0.9500	0.0580	0.1300	0.3900	0.0640
296	0.5400	0.2400	0.9600	0.4400	0.1200
297	3.3000	2.3000		3.7000	0.8700
298	2.0000	1.4000		1.9000	0.4300
299	1.5000	2.7000		2.9000	1.0000
300	2.8000	0.9500	3.9000	0.6200	0.4300
301	0.1400	0.3200	0.8300	0.6000	0.1200
302		2.3000			0.6500
303		0.8400	1.2000	0.9300	0.4700
304	2.9000	1.6000	1.5000	2.2000	0.9800
305		0.6700	1.1000	0.5500	0.2400
306	3.6000				
307	2.8000				
308	3.2000				
309	0.3570	0.1567	0.4200	0.4250	0.1450
310	0.4860	0.1380	0.3310	0.2150	0.0694
311	3.0000	1.4583		1.7567	1.1550
312		0.3299	2.6700	0.2680	0.1118
313	3.0400	0.3344	1.4800	0.3600	0.3093
314	2.1250	0.5200	2.3718	0.4290	0.1136
315		2.5800		2.1950	2.4450
316	0.4915	0.0625	0.2955	0.0924	0.0566
317	0.9777	0.0318	0.0817	0.0884	0.0423
318	0.4295	0.2890	1.2840	0.2160	0.0691
319	1.5493	0.1610	0.8551	0.1595	0.1064
320	1.6450	0.4515	2.6400	0.6690	0.3750
321	3.6400	1.1150	3.1557	1.2350	0.6480
322	0.6373	0.3000	0.5537	0.5970	0.2275
323	0.0715	0.0865	0.2500	0.0820	0.0530

Table 4 (cont'd)

Example	cdk4/D IC_{50} μM	cdk2/E IC_{50} μM	cdk2/A IC_{50} μM	cdk1/B IC_{50} μM	cdk5-HTS IC_{50} μM
324	0.2135	0.0530	0.1450	0.0825	0.0320
325	0.1650	0.0387	0.1255	1.4390	0.0395
326	2.0950	0.8200	2.4500	0.9950	0.4600
327	0.1890	0.0250	0.0670	0.0530	0.0310
328	0.6900	0.0353	0.0750	0.0800	0.0925
329	0.3150	0.2750	0.4250	0.3200	0.1600
330	2.1000	0.3700	1.1500	0.9400	0.4350
331	2.0000	0.9500	0.8750	0.4150	0.1600
332	2.0500	0.4167	1.3100	1.0500	0.5900
333	0.6700	0.3400	1.7000	1.3000	0.2600
334		0.9100	1650001.6500	1.3000	0.3000
335	1.6000	0.1600	1.1000	0.2500	0.3400
336	2.4000	0.1200	1.7000	0.3200	0.0740
337	0.4300	0.0250	0.1000	0.1500	0.1500
338	0.2700	0.1700	0.3400	0.5700	0.0480
339		1.8000			0.8300
340	0.3100	0.3500	0.9600	1.3000	0.1700
341	0.4200	0.2800	0.8900	0.5200	0.0920
342	2.2000	0.3700	1.8000		1.4000
343		0.1200	0.2900	0.2800	0.1100
344	0.3700	0.4700	0.9900	0.3600	0.0460
345	0.1600	0.4300	0.8300	0.5900	0.1600
346	0.3100	0.2600	0.4500	0.0610	0.0290
347	0.0580	0.1200	0.5800	0.1400	0.0350
348	0.0140	0.0490	0.1700	0.0620	0.0130
349		0.5300	1.1000	0.8800	0.2000
350		1.2000		3.1000	0.2300
351	1.2000	0.5600	1.3000	0.7000	0.3100
352					2.9000

Table 4 (cont'd)

Example	cdk4/D IC_{50} μM	cdk2/E IC_{50} μM	cdk2/A IC_{50} μM	cdk1/B IC_{50} μM	cdk5-HTS IC_{50} μM
353		0.3200	0.4600	0.7100	0.2300
354	0.9100	1.2000	1.1000	1.6000	0.7700
355		0.6800	1.1000	0.5000	0.3000
356	0.2900	0.5100	0.4700	0.4100	0.0610
357	0.3600	0.7000	1.6000	2.1000	0.2900
358	0.3000	0.1800	0.0830	0.1600	0.0900
359	1.8000	0.4500	0.4300	0.3900	0.1800
360	0.3900	0.9900	1.0000	0.3400	0.0860
361	0.3500	0.4400	0.3100	0.1800	0.1500
362			4.0000	0.2700	0.1900
363	1.9000				
364	0.2400	0.0603	0.2550	0.2000	0.0875
365	0.4750	0.1220	0.4465	0.2045	0.0598
366		0.2547	0.8815	1.3250	0.6995
367	2.3000				
368	3.0100	0.8355	3.0650	1.3600	0.7235
369	0.5260	0.0719	0.2873	0.1293	0.0853
370	1.1360	1.2800	0.6100	0.8082	0.9167
371	0.3310	0.2865	0.6990	0.3725	0.2345
372		1.0260		2.4000	2.2653
373	2.1500	0.2080	1.1533	0.4300	0.2140
374	2.9400	0.6680	2.8798	0.9490	0.3788
375	0.7200	0.0489	0.4075	0.1066	0.0847
376	0.3805	0.3995	1.1770	0.2750	0.1310
377	0.5095	0.2283	1.1005	0.3135	0.2011
378	0.0975	0.0860	0.3400	0.1500	0.0965
379	0.1400	0.0273	0.0840	0.0430	0.0465
380	0.2850	0.0260	0.0830	0.0590	0.0325
381	0.4000	0.1330	0.5150	0.1500	0.2050

Table 4 (cont'd)

Example	cdk4/D IC_{50} μM	cdk2/E IC_{50} μM	cdk2/A IC_{50} μM	cdk1/B IC_{50} μM	cdk5-HTS IC_{50} μM
382	0.6700	0.3200	1.5500	1.3000	0.5900
383	0.1600	0.0253	0.0965	0.0455	0.0465
384	1.1300	0.0257	0.0985	0.1150	0.0915
385	1.1450	0.1500	0.3200	0.1550	0.1300
386	0.6200	0.0907	0.2000	0.0830	0.0235
387	0.2850	0.0800	0.1600	0.1285	0.1080
388	0.3100	0.1000	0.6900	0.2000	0.1100
389		0.3200	0.8700	0.4500	0.2000
390	1.1000	0.0850	0.4700	0.2200	0.0840
391	0.5150	0.0650	1733333.7833	0.1650	0.0580
392	0.7600	0.0770	0.3600	0.1400	0.1100
393	0.1800	0.0110	0.0340	0.0450	0.0097
394	0.1200	0.1200	0.3400	0.3600	0.1500
395	0.0900	0.0850	0.3400	0.2200	0.0910
396	1.1000	0.3000	2.6000	0.6000	0.5900
397	0.2500	0.0750	0.3100	0.2900	0.0810
398	0.2300	0.3500	1.4000	0.4200	0.0880
399	0.9200	0.0500	0.3100	0.0630	0.0140
400	0.1700	0.0560	0.4800	0.1200	0.0380
401	1.3000	0.8600	0.8800	1.9000	0.2920
402	0.0870	0.0250	0.1400	0.0580	0.0200
403	0.0930	0.0390	0.2300	0.0730	0.0230
404	1.9000	0.3000	0.6500	0.6100	0.2800
405	3.1000				
406	0.2600	0.0947	0.1600	0.1135	0.0525
407	0.9800	0.6800	0.4600	0.3200	0.0560
408	0.1300	0.1100	0.1500	0.1900	0.0130
409	0.0440	0.0993	0.2600	0.2600	0.0540
410	0.1515	0.0880	0.1350	0.2450	0.0445

Table 4 (cont'd)

Example	cdk4/D IC_{50} μM	cdk2/E IC_{50} μM	cdk2/A IC_{50} μM	cdk1/B IC_{50} μM	cdk5-HTS IC_{50} μM
411	0.1800	0.2000	0.2625	0.2725	0.1770
412	2.0000	0.5120	0.7133	0.7150	0.2775
413	0.1800	0.0523	0.1385	0.0680	0.0435
414	0.0510	0.0910	0.1550	0.1650	0.0385
415	0.4900	0.2400	1.1000	1.1000	0.2900
416	0.1800	0.2200	0.3500	0.2800	0.0380
417	3.4000	0.5900	0.8700	0.8800	0.1700
418	0.1300	0.0270	0.0330	0.0900	0.0150
419	0.2600	0.1200	1400000.1400	0.1400	0.0330
420	1.0000	1.0000		1.4000	0.6600
421	1.9000	3.9000	0.9200	0.7000	0.0830
422	0.0660	0.1700	0.1700	0.1600	0.0097
423		1.1000	2.6000	1.8000	0.1600
424	0.1000	0.3600	0.4600	0.5200	0.0390
425	0.8500	0.7700	1.8000	0.4900	0.1800
426	0.0580	0.1300	0.2100	0.3100	0.0210
427	0.1400	0.1600	0.5900	0.1600	0.0210
428	2.4000	2.4000		2.6000	0.8900
429	0.5600	0.1200	0.8600	0.2300	0.0390
430	0.0350	0.0950	0.2400	0.1800	0.0150
431	0.1400	0.1200	0.3000	0.1700	0.0230
432	0.1500	0.3900	0.4200	0.5400	0.0600
433	0.2500	0.2300	0.1600	0.4800	0.0760
434	0.3500	0.5200	0.4000	0.4700	0.0540
435	2.6000				1.3000
436	1.8000	0.3400	0.7300		0.9700
437	3.2000				
438	1.1150	0.6900	0.3800	0.9550	0.2155
439	0.3100		0.6300	0.4000	0.1200

Table 4 (cont'd)

Example	cdk4/D IC_{50} μM	cdk2/E IC_{50} μM	cdk2/A IC_{50} μM	cdk1/B IC_{50} μM	cdk5-HTS IC_{50} μM
440	0.1500	1.5000	1.1000	1.4000	0.4400
441	0.8900	0.4700	0.2900	0.2900	0.1500
442	3.6000	3.6000	1.7000	1.9000	0.4400
443	0.3200	0.1700	0.2000	0.5200	0.0710
444	0.3600	0.7100	0.0750	0.5300	0.0630
445	2.7000				
446	0.1675	0.1767	0.2150	0.3400	0.0745
447	0.0445	0.0607	0.1450	0.0895	0.0190
448	0.0460	0.0200	0.0520	0.0265	0.0085
449	0.1285	0.0173	0.0410	0.0775	0.0078
450	0.1125	0.1300	0.2650	0.1400	0.0645
451	0.4500	0.2400	0.5550	0.5900	0.1330
452	0.1145	0.0220	0.0400	0.0255	0.0130
453	0.3300	0.0527	0.1050	0.0515	0.0370
454	0.2620	0.0683	0.1150	0.0595	0.0215
455	0.1100	0.4633	0.1700	0.0985	0.0505
456	0.1300	0.1100	0.3100	0.1300	0.0250
457	2.4000	0.2500	0.7600	0.3400	0.2800
458	1.7000	0.1000	0.2800	0.1500	0.0290
459	0.2160	0.3162	1.2045	0.4910	0.1961
460	0.1600	0.0730	0.2600	0.1400	0.0360
461	0.5500	0.7800	1.8000	0.4600	0.0820
462		0.0600	0.0780	0.0880	0.0100
463	0.2500	0.6600	2.0000	0.3000	0.1800
464	0.1500	0.1300	0.3100	0.1700	0.0170
465	0.1000	0.0560	0.2600	0.0760	0.0088
466	1.5000	1.4000		1.3000	0.3100
467	0.0960	0.0970	0.2700	0.1900	0.0080
468	0.9500	0.3300	0.5300	0.3400	0.0265

Table 4 (cont'd)

Example	cdk4/D IC_{50} μM	cdk2/E IC_{50} μM	cdk2/A IC_{50} μM	cdk1/B IC_{50} μM	cdk5-HTS IC_{50} μM
469	0.0300	0.0460	0.2400	0.0900	0.0096
470	0.1100	0.0500	0.1500	0.0670	0.0061
471	0.1200	0.2200	0.5300	0.3400	0.0490
472	0.3700	0.2000	0.1500	0.2500	0.0520
473	0.5100	0.4700	0.3300	0.4000	0.0670
474	0.2100	0.1400	0.1100	0.2400	0.0410
475	1.4000	0.8200	1.5000	1.1000	0.4800
476	0.2300	0.2000	0.1600	0.1700	0.0310
477		0.2600	0.3700	0.1700	0.0380
478	1.3000				
479	1.7000				
480	2.9000				
481	0.9381	0.0693	0.4183	0.1339	0.0391
482	0.1664	0.1525	0.5970	0.2139	0.0632
483	1.3295	0.3535	1.6704	0.7315	0.1690
484	0.1867	0.1355	0.3627	0.1917	0.0408
485	0.2320	0.1312	0.6005	0.2414	0.6472
486	1.0308	0.4670	0.9200	0.2176	0.0828
487	0.6923	0.2100	0.7283	0.1770	0.0768
488	2.2450	0.4940	1.9787	0.4460	0.1245
489					3.5000
490	0.3495	0.0797	0.7527	0.0867	0.0492
491	0.2599	0.1793	0.4360	0.1510	0.0444
492	0.1245	0.1633	0.6000	0.1450	0.0860
493	0.0250	0.0120	0.0505	0.0145	0.0087
494	0.2300	0.1267	0.4400	0.1020	0.0720
495	0.5700	0.1467	0.6500	0.2150	0.1075
496	0.2800	0.0310	0.0895	0.0240	0.0175
497	0.4800	0.0800	0.1600	0.0465	0.0555

Table 4 (cont'd)

Example	cdk4/D IC_{50} μM	cdk2/E IC_{50} μM	cdk2/A IC_{50} μM	cdk1/B IC_{50} μM	cdk5-HTS IC_{50} μM
498	0.1700	0.0470	0.2000	0.0495	0.0680
499	0.1925	0.0463	0.1150	0.0460	0.0125
500	0.0980	0.0740	0.3400	0.1100	0.0160
501		0.2400	0.7600	0.2800	0.0810
502	0.3500	0.0680	0.3600	0.1000	0.0210
503	0.1700	0.0360	1550000.1550	0.0790	0.0130
504	0.2100	0.3800		0.5200	0.3700
505	0.0340	0.0670	0.2200	0.0730	0.0140
506	0.0360	0.0930	0.4000	0.1100	0.0440
507	0.1500	0.3100	1.3000	0.3300	0.0640
508	0.1400	0.2800	2.1000	0.2300	0.0700
509	0.0980	0.0640	0.2400	0.1900	0.0260
510	0.2700	0.2100	0.3100	0.1800	0.1200
511	0.2200	0.1600	0.2900	0.1400	0.0500
512	2.2000	0.0560	0.1200	0.0390	0.0830
513	0.8300	0.3300	0.6300	0.1600	0.1100
514	0.2500	3.1000		2.0000	1.1000
515	0.2000	0.2300	0.6700	0.4800	0.0710
516	0.0280	0.0950	0.2800	0.0620	0.0330
517	0.1300	0.0290	0.0560	0.0620	0.0180
518	0.3645	0.0530	0.0575	0.0315	0.0175
519	0.1500	0.1400	0.3100	0.0470	0.0330
520	0.1200	0.0410	0.0860	0.0510	0.0098
521	0.0670	0.0980	0.2200	0.0670	0.0420
522	0.3600	0.3200	1.6000	1.1000	0.3000
523	0.3900	0.0460	0.1600	0.0930	0.0280
524	2.0000	0.4500	0.6500	0.6200	0.2900
525	1.2000	0.1100	0.2900	0.0990	0.0270
526	0.0850	0.2000	0.1600	0.1400	0.0880

Table 4 (cont'd)

Example	cdk4/D IC_{50} μM	cdk2/E IC_{50} μM	cdk2/A IC_{50} μM	cdk1/B IC_{50} μM	cdk5-HTS IC_{50} μM
527					
528	0.0127	0.0465	0.0740	0.0345	0.0363
529	0.0310	0.0240	0.0355	0.0825	0.0320
530	1.7000	0.1800	0.2500	0.2200	0.0990
531	0.0510	0.1000	0.0740	0.1700	0.0500
532	1.5000	0.6300	0.7800	0.5100	0.2100
533	0.1500	0.1400	0.3300	0.2500	0.0660
534	0.3400	0.0810	0.3400	0.1900	0.0450
535	0.0635	0.0887	0.2200	0.1450	0.0740
536	0.0250	0.0140	0.0315	0.0185	0.0197
537	0.0420	0.0085	0.0255	0.0495	0.0123
538	0.3380	0.0727	0.3200	0.4250	0.1450
539	0.0235	0.0143	0.0335	0.0280	0.0235
540	0.7100	0.0617	0.1700	0.3100	0.2000
541	0.1100	0.0223	0.0415	0.0595	0.0135
542	0.0095	0.0350	0.0750	0.0850	0.0077
543	0.2800	0.5000	1.7000	0.5500	0.2100
544	0.1200	0.0820	0.3500	0.0850	0.0230
545	0.0550	0.1400	0.3100	0.1800	0.0250
546	1.3950	0.4150	1.3450	0.5550	0.0640
547	0.0540	0.1100	0.5900	0.3000	0.0660
548	0.1800	0.1800	0.2000	0.2900	0.0990
549	0.0700	0.2900	0.1900	0.2000	0.0590
550	0.3100	0.1100	0.2000	0.5100	0.1900
551	0.2900	0.0160	0.0140	0.0360	0.0550
552	0.1800	0.1500	0.2100	0.0480	0.0540
553	0.0990			2.5000	
554	0.2300	0.1515	0.1480	0.1695	0.0320
555	0.0690	0.0990	0.1600	0.2200	0.0600

Table 4 (cont'd)

Example	cdk4/D IC_{50} μM	cdk2/E IC_{50} μM	cdk2/A IC_{50} μM	cdk1/B IC_{50} μM	cdk5-HTS IC_{50} μM
556	0.0190	0.0400	0.0160	0.0300	0.0090
557	0.1200		0.1300	0.0730	0.0960
558	0.0300	0.2800	0.3400	0.5100	0.2200
559	0.2700	0.0910	0.0870	0.0820	0.0940
560	0.9100	0.3700	0.2200	0.4500	0.4900
561	0.4800	0.1500	0.2200	0.3500	0.4400
562	0.1600	0.1400	0.0560	0.0470	0.0500
563	0.0870	0.1027	0.3200	0.1560	0.0865
564	0.5050	0.0500	0.1175	0.0945	0.0520
565	0.3850	0.1933	0.5100	0.3650	0.2900
566	0.8550	0.1867	0.6150	0.4450	0.2550
567	0.1450	0.0163	0.0545	0.0760	0.0315
568	0.9200	0.0430	0.1025	0.1010	0.1020
569	3.5000	0.2600	1.6000	0.5600	0.3100
570	0.6800	0.0630	0.4300	0.1700	0.0500
571	0.0650	0.0051	0.0150	0.0290	0.0088
572	0.1200	0.0840	0.5300	0.4300	0.1900
573	0.1900	0.1800	0.8200	0.2600	0.1000
574	0.0800	0.2700	0.5200	0.2900	0.1400
575	0.5400	0.2800	0.3300	0.3300	0.2300
576	0.4200	0.4600	0.4900	0.6500	0.4100
577	0.2300	0.1100	0.1200	0.1200	0.0920
578	0.1400	0.1700	0.1900	0.3100	0.1100
579	2.8000	2.9000	3.9000		
580	0.5500	0.1300	0.2700	0.0790	0.1300
581	0.4200			1.6000	
582	0.6600	0.2500	0.4400	0.2800	0.1900
583	1.3000	0.2000	0.2600	0.3550	0.1050
584	0.0980	0.1000	0.1400	0.1700	0.0390

Table 4 (cont'd)

Example	cdk4/D IC_{50} μM	cdk2/E IC_{50} μM	cdk2/A IC_{50} μM	cdk1/B IC_{50} μM	cdk5-HTS IC_{50} μM
585	0.2100	0.3200	0.1800	0.3400	0.4500
586	0.4900	0.2000	0.1700	0.1200	0.1700
587	0.2000	0.0810	0.4400	0.3600	0.1600
588	2.6000	0.1000	0.6700	0.7100	0.2600
589		0.1900	0.7100	1.3000	0.5700
590	0.4600		0.3200	0.6500	0.1600
591	0.2100	1.8000		3.9000	0.1400
592	0.2000	0.0710	0.3100	0.4300	0.2300
593	0.9050	1.3667	2.7000	0.9600	0.6950
594		1.6667		1.9000	0.5550
595	2.0000	0.5100	1.4500	1.9950	0.1550
596		1.3000		1.8550	0.7200
597	2.0000	0.3167	1.0050	0.4350	0.2500
598		0.5233	0.9700	0.4550	0.5250
599		1.7000		2.3500	0.7850
600	1.7750	0.9700	1.6000	0.9050	0.1235
601	1.4500	1.1967	2.8500	1.6500	0.4000
602	1.3000			1.8000	0.1800
603					1.2000
604	3.2000				2.0000
605					
606	3.8000			3.5000	1.8000
607	1.4000				0.6100
608					
609					3.2000
610					
611					3.3000
612					
613	0.4150	0.0363	0.1525	0.1010	0.0630

Table 4 (cont'd)

Example	cdk4/D IC_{50} μM	cdk2/E IC_{50} μM	cdk2/A IC_{50} μM	cdk1/B IC_{50} μM	cdk5-HTS IC_{50} μM
614	1.3500	0.9167	2.0000	1.4300	0.6150
615	3.0000	1.5333	3.6000	1.7600	1.1400
616		3.8000			2.2000
617		2.9000		1.7000	0.5950
618					
619					1.7000
620					0.4200
621	0.2300	0.4000	0.9250	0.5400	0.2500

The invention compounds can be formulated in conventional manners to provide convenient dosage forms for delivery to mammals by various routes, including oral, parenteral (ie, subcutaneous, intravenous, and intramuscular), transdermal, eg, slow release skin patch or cream, as well as by slow release delivery devices such as osmotic pumps, suppositories, and buccal seals. The following examples further illustrate how the compounds are readily formulated.

EXAMPLE 625

50 mg Tablet Formulation

Per Tablet		Per 10,000 Tablets
0.050 g	2-phenylamino-8-(1-ethylpropyl)-8H-pyrido[2,3-d]pyrimidin-7-one	500 g
0.080 g	Lactose	800 g
0.010 g	cornstarch (for mix)	100 g
0.008 g	cornstarch (for paste)	80 g
0.148 g		1480 g
0.002 g	magnesium stearate (1%)	20 g
0.150 g		1500 g

The pyrido pyrimidine, lactose, and cornstarch (for mix) are blended to uniformity. The cornstarch (for paste) is suspended in 600 mL of water and heated with stirring to form a paste. This paste is used to granulate the mixed powders. The wet granules are passed through a No. 8 hand screen and dried at 80°C. The dry granules are then passed through a No. 16 screen. The mixture is lubricated with 1% magnesium stearate and compressed into tablets in a conventional tableting machine. The tablets are useful for treating neurodegenerative diseases, especially Alzheimer's disease.

EXAMPLE 626

Preparation of Oral Suspension

Ingredient	Amount
8-Ethyl-2-(3,4-dimethoxyphenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one	500 mg
Sorbitol solution (70% N.F.)	40 mL
Sodium benzoate	150 mg
Saccharin	10 mg
Cherry flavor	50 mg
Distilled water qs	100 mL

The sorbitol solution is added to 40 mL of distilled water, and the pyrido pyrimidine is suspended therein. The saccharin, sodium benzoate, and flavoring are added and dissolved. The volume is adjusted to 100 mL with distilled water. Each milliliter of syrup contains 5 mg of invention compound. The formulation is ideal for treating neurodegenerative diseases, especially ALS.

EXAMPLE 627

Preparation of Parenteral Solution

In a solution of 700 mL of propylene glycol and 200 mL of water for injection is suspended 20.0 g of 8-methyl-2-phenylamino-8H-pyrido[2,3-d]-pyrimidin-7-one with stirring. After suspension is complete, the pH is adjusted to 5.5 with hydrochloric acid, and the volume is made up to 1000 mL with water

for injection. The formulation is sterilized, filled into 5.0 mL ampoules, each containing 2.0 mL (representing 40 mg of invention compound) and sealed under nitrogen.

EXAMPLE 628

Suppositories

A mixture of 400 mg of 8-ethyl-2-(4-fluoro-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one, and 600 mg of theobroma oil is stirred at 60°C to uniformity. The mixture is cooled and allowed to harden in a tapered mold to provide a 1 g suppository.

EXAMPLE 629

Slow Release Formulation

Five hundred milligrams of 8-(isopropyl)-2-(3-nitro-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one is converted to a hydrochloride salt and placed into an Oros osmotic pump for controlled release for treatment of Huntington's disease.

EXAMPLE 630

Skin Patch Formulation

Fifty milligrams of 8-isopropyl-2-(4-hydroxyphenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one is admixed with 50 mg of propylene glycol monolaurate in a polydimethylsiloxane adhesive. The mixture is layered onto an elastic film made with an adhesive formulation of polybutene, polyisobutylene, and propylene glycol monolaurate. The layers are placed between 2 layers of polyurethane film. A release liner is attached to the adhesive surface, and is removed prior to application to a skin surface. The propylene glycol monolaurate serves as a permeation-enhancing agent. This controlled release patch formulation is ideal for treating elderly patients suffering from neurodegenerative diseases such as Alzheimer's disease and Parkinson's disease.

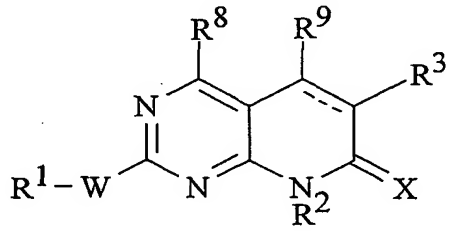
CLAIMS

What is claimed is:

1. A method for treating a mammal suffering from a neurodegenerative disease and in need of treatment comprising administering an effective amount of a cyclin-dependent kinase inhibitor.

2. The method according to Claim 1 wherein the cyclin-dependent kinase inhibitor inhibits cdk5 more than any other cyclin-dependent kinase enzyme.

3. A method for treating a mammal suffering from a neurodegenerative disease and in need of treatment comprising administering an effective amount of a cyclin-dependent kinase inhibitor which is a compound of Formula I



I

or a pharmaceutically acceptable salt thereof, wherein:
the dotted line represents an optional double bond;
W is NH, S, SO, or SO_2;
X is either O or NH;
R^1 and R^2 are independently selected from the group consisting of H, $(CH_2)_nAr$, $(CH_2)_n$heteroaryl, $(CH_2)_n$heterocyclyl, C_1-C_{10} alkyl, C_3-C_{10} cycloalkyl, C_2-C_{10} alkenyl, and C_2-C_{10} alkynyl, wherein n is 0, 1, 2, or 3, and the $(CH_2)_nAr$, $(CH_2)_n$heteroaryl, alkyl, cycloalkyl, alkenyl, and alkynyl groups are optionally substituted by up to 5 groups selected from NR^4R^5, $N(O)R^4R^5$, $NR^4R^5R^6Y$, phenyl, substituted phenyl, hydroxy, alkoxy,

phenoxy, thiol, thioalkyl, halo, COR^4, CO_2R^4, $CONR^4R^5$, $SO_2NR^4R^5$, SO_3R^4, PO_3R^4, aldehyde, nitrile, nitro, heteroaryloxy, $T(CH_2)_mQR^4$, $C(O)T(CH_2)_mQR^4$, $NHC(O)T(CH_2)_mQR^4$, or $T(CH_2)_mCO_2R^4$ wherein m is 1-6, T is O, S, NR^4, $N(O)R^4$, NR^4R^6Y, or CR^4R^5, and Q is O, S, NR^5, $N(O)R^5$, or NR^5R^6Y;

R^3 is H or alkyl;

R^4 and R^5 are independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, substituted alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, $(CH_2)_nAr$, C_3-C_{10} cycloalkyl, heterocyclyl, and heteroaryl, or R^4 and R^5 together with the nitrogen to which they are attached optionally form a ring having 3 to 7 carbon atoms and said ring optionally contains 1, 2, or 3 heteroatoms selected from the group consisting of nitrogen, substituted nitrogen, oxygen, and sulfur;

R^6 is alkyl;

R^8 and R^9 independently are H, C_1-C_3alkyl, NR^4R^5, $N(O)R^4R^5$, $NR^4R^5R^6Y$, hydroxy, alkoxy, thiol, thioalkyl, halo, COR^4, CO_2R^4, $CONR^4R^5$, $SO_2NR^4R^5$, SO_3R^4, PO_3R^4, CHO, CN, or NO_2; and

Y is a halo counter-ion.

4. The method according to Claim 3 wherein the compound administered has Formula I wherein W is NH and R^8 and R^9 both are hydrogen.

5. The method according to Claim 4 wherein the compound administered has Formula I wherein a double bond exists between C_5 and C_6, and X is O.

6. The method according to Claim 5 wherein the compound administered has Formula I wherein R^1 is phenyl or substituted phenyl.

7. The method according to Claim 6 wherein the compound administered has Formula I wherein R^2 is an alkyl, substituted alkyl, or cycloalkyl unsubstituted or substituted.

8. The method according to Claim 7 whereas the compound administered is selected from:

8-Ethyl-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Benzyl-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

7-Oxo-2-phenylamino-7H-pyrido[2,3-d]pyrimidin-8-yl)-acetic acid methyl ester;

8-Methoxymethyl-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(3-Benzyloxypropyl)-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Oxiranylmethyl-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Butyl-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

2-Phenylamino-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Isobutyl-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Isopropyl-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(Biphenyl-4-ylamino)-8-ethyl-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Ethyl-2-(pyridin-4-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Ethyl-2-(4-methoxyphenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-[4-(2-Diethylaminoethoxy)-phenylamino]-8-ethyl-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Ethyl-2-[4-(4-methylpiperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Ethyl-2-[3-(1,1,2,2-tetrafluoroethoxy)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Ethyl-2-(4-hydroxyphenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-Benzyloxyphenylamino-8-ethyl-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Ethyl-2-[4-(2-methoxyethoxy)phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(4-Methoxybenzyl)-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

2-[4-(2-Diethylaminoethoxy)-phenylamino]-8-isopropyl-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Isopropyl-2-[4-(4-methylpiperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Methyl-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

2-Amino-8-methyl-8H-pyrido[2,3-d]pyrimidin-7-one;

2-Benzylamino-8-methyl-8H-pyrido[2,3-d]pyrimidin-7-one;

2-Butylamino-8-methyl-8H-pyrido[2,3-d]pyrimidin-7-one;

2-Ethylamino-8-methyl-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Methyl-2-(2-pyridin-2-yl-ethylamino)-8H-pyrido[2,3-d]-pyrimidin-7-one;

2-Isopropylamino-8-methyl-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1-Ethylpropyl)-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Isopentyl-2-methanesulfanyl-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1-Ethylpropyl)-2-methanesulfinyl-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1-Ethylpropyl)-2-[4-(4-methylpiperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(4-Diethylamino-phenylamino)-8-ethyl-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-Ethyl-2-(4-morpholin-4-yl-phenylamino)-8H-pyrido[2,3-d]-pyrimidin-7-one;

6-Methyl-2-methylsulfanyl-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Ethyl-6-methyl-2-methylsulfanyl-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Ethyl-2-methanesulfinyl-6-methyl-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Ethyl-6-methyl-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Ethyl-6-methyl-2-[4-(4-methyl-piperazin-1-yl)-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Sec-butyl-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(2-Methoxyethyl)-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(3-Phenoxypropyl)-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Ethyl-2-(4-fluorophenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Ethyl-2-(3-fluorophenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Ethyl-2-(3-fluoro-4-methoxyphenylamino)-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-Ethyl-2-(3-fluoro-2-methoxyphenylamino)-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-Ethyl-2-(2-methoxyphenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(4-Dimethylamino-phenylamino)-8-ethyl-8H-pyrido[2,3-d]-pyrimidin-7-one;

2-Phenylamino-8-phenyl-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(4-Hydroxy-phenylamino)-8-isopropyl-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-Isopropyl-2-(4-methoxy-phenylamino)-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-Ethyl-2-(4-pyrrol-1-yl-phenylamino)-8H-pyrido[2,3-d]-pyrimidin-7-one;

2-[4-(4-Methyl-piperazin-1-yl)-phenylamino]-8-phenyl-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(3-Benzyloxy-propyl)-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(3-Benzyloxy-propyl)-2-[4-(2-diethylamino-ethoxy)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(3-Benzyloxy-propyl)-2-(4-dimethylamino-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(2-Benzyloxy-ethyl)-2-[4-(2-diethylamino-ethoxy)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Isopropyl-2-[4-(2-morpholin-4-yl-ethoxy)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(2-Benzyloxy-ethyl)-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

2-[4-(2-Diethylamino-ethoxy)-phenylamino]-8-[3-(tetrahydro-pyran-2-yloxy)-propyl]-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(4-Piperidin-1-yl-phenylamino)-8-[3-(tetrahydro-pyran-2-yloxy)-propyl]-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Cyclohexylmethyl-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Cyclohexylmethyl-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(3-Benzyloxy-propyl)-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(3-Hydroxy-propyl)-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one dihydrochloride;

8-(2,2-Dimethyl-2-(tetrahydro-pyran-2-yloxy)propyl]-2-(4-piperidin-1-yl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Ethyl-2-[4-(pyridin-3-yloxy)-phenylamino]-8H-pyrido[2,3-d]-pyrimidin-7-one;

2-[4-(1H-Benzoimidazol-2-yl)-phenylamino]-8-ethyl-8H-pyrido[2,3-d]pyrimidin-7-one;

2-[4-(Benzyloxy-phenylamino]-8-ethyl-8H-pyrido[2,3-d]-pyrimidin-7-one;

N-{2-[4-(8-Ethyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-phenyl]-2-hydroxy-1-hydroxymethyl-ethyl}-acetamide;

8-Ethyl-2-[4-(4-methyl-piperidine-1-carbonyl)-phenylamino]-8H-pyrido[2,3-d]pyrimidin-7-one;

3-(8-Ethyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-benzamide;

2-(3,4-Dimethoxy-phenylamino]-8-ethyl-8H-pyrido[2,3-d]-pyrimidin-7-one;

8-Ethyl-2-(4-hydroxy-3-methoxy-phenylamino]-8H-pyrido[2,3-d]-pyrimidin-7-one;

2-[4-(2,3-Dihydroxy-propoxy)-phenylamino]-8-ethyl-8H-pyrido[2,3-d]pyrimidin-7-one;

2-[4-(2-Diethylamino-ethylamino)-phenylamino]-8-ethyl-8H-pyrido[2,3-d]pyrimidin-7-one;

N-[4-[2-[4-[(8-Ethyl-7,8-dihydro-7-oxopyrido[2,3-d]pyrimidin-2-yl)amino]phenoxy]ethoxy]phenyl]propanediimidamide;

2-[3-(1H-Benzoimidazol-2-yl)-phenylamino]-8-ethyl-8H-pyrido[2,3-d]pyrimidin-7-one;

3-(8-Ethyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-N,N-dimethyl-benzamide; and

8-Ethyl-6-methyl-2-{4-[4-(3-morpholin-4-yl-propyl)-piperidin-1-yl]-phenylamino}-8H-pyrido[2,3-d]pyrimidin-7-one.

9. A method for treating a mammal suffering from a neurodegenerative disease and in need of treatment comprising administering an effective amount of a cyclin-dependent kinase inhibitor, wherein the neurodegenerative disease is Alzheimer's disease.

10. A method for treating a mammal suffering from a neurodegenerative disease and in need of treatment comprising administering an effective amount of a cyclin-dependent kinase inhibitor, wherein the neurodegenerative disease is Huntington's disease.

11. A method for treating a mammal suffering from a neurodegenerative disease and in need of treatment comprising administering an effective amount of a cyclin-dependent kinase inhibitor, wherein the neurodegenerative disease is Parkinson's disease.

12. A compound selected from:

8-Methyl-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Ethyl-2-(1H-indazol-5-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(1H-Benzotriazol-5-ylamino)-8-ethyl-8H-pyrido[2,3-d]pyrimidin-7-one;

[4-(8-Ethyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-phenyl]-carbamic acid tert-butyl ester;

8-Ethyl-2-(2-fluoro-4-hydroxy-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(3-Chloro-4-hydroxy-phenylamino)-8-ethyl-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(3,5-Dichloro-4-hydroxy-phenylamino)-8-ethyl-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Ethyl-2-(3,4,5-trimethoxy-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Ethyl-2-(4-fluoro-3-trifluoromethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Ethyl-2-(4-fluoro-3-methyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

4-(8-Ethyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-benzenesulfonamide;

2-(3-Hydroxy-4-methoxy-phenylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Ethyl-2-(2-fluoro-5-nitro-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

4-(8-Ethyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-phthalonitrile;

N-[2-Cyano-5-(8-ethyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-phenyl]-acetamide;

8-Ethyl-2-(3-methoxy-5-trifluoromethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(3,4-Difluoro-phenylamino)-8-ethyl-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Ethyl-2-(2-fluoro-5-trifluoromethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(3,5-Difluoro-phenylamino)-8-ethyl-8H-pyrido[2,3-d]pyrimidin-7-one;

4-(8-Ethyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-benzonitrile;

8-Ethyl-2-(3-trifluoromethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(3-Bromo-4-trifluoromethoxy-phenylamino)-8-ethyl-8H-pyrido[2,3-d]pyrimidin-7-one;

N-[5-(8-Ethyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-2-methyl-phenyl]-methanesulfonamide;

N-[2-Cyano-4-(8-ethyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-phenyl]-acetamide;

2-Phenylamino-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(3-Chloro-4-methoxy-phenylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(2-Fluoro-5-trifluoromethyl-phenylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(4-Chloro-3-trifluoromethyl-phenylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Propyl-2-(3-trifluoromethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(4-Bromo-3-trifluoromethyl-phenylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(3,5-Bis-trifluoromethyl-phenylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(3-Iodo-phenylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one;

4-(7-Oxo-8-propyl-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-benzenesulfonamide;

2-(3,4-Dimethyl-phenylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(2-Fluoro-4-nitro-phenylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(2,4-Difluoro-phenylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one;

4-(7-Oxo-8-propyl-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-benzonitrile;

2-(1H-Indol-5-ylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(1H-Indazol-5-ylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(1H-Benzotriazol-5-ylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one;

[4-(7-Oxo-8-propyl-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-phenyl]-carbamic acid tert-butyl ester;

2-(3-Chloro-4-hydroxy-phenylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(3,5-Dichloro-4-hydroxy-phenylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(4-Methoxy-phenylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(3-Nitro-phenylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(3,4-Dimethoxy-phenylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(4-Fluoro-phenylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(2-Fluoro-5-nitro-phenylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Propyl-2-(3,4,5-trimethoxy-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(4-Fluoro-3-trifluoromethyl-phenylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(3-Hydroxy-4-methoxy-phenylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(4-Fluoro-3-methyl-phenylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(3-Fluoro-4-methoxy-phenylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one;

4-(7-Oxo-8-propyl-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-phthalonitrile;

N-[2-Cyano-5-(7-oxo-8-propyl-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-phenyl]-acetamide;

2-(4-Bromo-3-chloro-phenylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(3-Methoxy-5-trifluoromethyl-phenylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(3,4-Difluoro-phenylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(3-Chloro-4-iodo-phenylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one;

N-Methyl-N-[4-(7-oxo-8-propyl-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-phenyl]-acetamide;

2-(3,5-Dimethyl-phenylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(3-Chloro-4-methyl-phenylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one;

3-(7-Oxo-8-propyl-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-benzenesulfonamide;

2-(3,5-Difluoro-phenylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(3,4-Dichloro-phenylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(4-Fluoro-3-nitro-phenylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(2,3-Dihydro-1H-indol-6-ylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one;

N-[3-(7-Oxo-8-propyl-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-phenyl]-acetamide;

2-(4-Hydroxy-3-methyl-phenylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(4-Hydroxy-3-morpholin-4-ylmethyl-phenylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(2,3-Dimethyl-2,3-dihydro-1H-indol-5-ylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(2,3-Dihydro-1H-indol-5-ylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(1H-Indazol-6-ylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Propyl-2-(3,4,5-trifluoro-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(4-Bromo-3-methyl-phenylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Propyl-2-(4-trifluoromethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Propyl-2-(4-trifluoromethoxy-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(3-Bromo-4-trifluoromethoxy-phenylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Butyl-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Butyl-2-(3-chloro-4-methoxy-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Butyl-2-(2,4,6-trifluoro-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Butyl-2-(2-fluoro-4-nitro-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Butyl-2-(2,4-difluoro-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(3-Chloro-4-fluoro-phenylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one;

N-[4-(8-Butyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-phenyl]-N-methyl-acetamide;

4-(8-Butyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-benzamide;

8-Butyl-2-(2-fluoro-5-trifluoromethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Butyl-2-(3-trifluoromethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(4-Bromo-3-trifluoromethyl-phenylamino)-8-butyl-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Butyl-2-(3-iodo-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(3-Fluoro-4-methyl-phenylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Butyl-2-(3,4-dimethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Butyl-2-(1H-indol-5-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Butyl-2-(1H-indazol-5-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(1H-Benzotriazol-5-ylamino)-8-butyl-8H-pyrido[2,3-d]pyrimidin-7-one;

[4-(8-Butyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-phenyl]-carbamic acid tert-butyl ester;

8-Butyl-2-(2-fluoro-4-hydroxy-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Butyl-2-(3-chloro-4-hydroxy-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Butyl-2-(3,5-dichloro-4-hydroxy-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Butyl-2-(4-methoxy-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Butyl-2-(3,4-dimethoxy-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Butyl-2-(4-fluoro-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Butyl-2-(4-chloro-3-methyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Butyl-2-(3,4,5-trimethoxy-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Butyl-2-(4-fluoro-3-trifluoromethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Butyl-2-(3,5-dichloro-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Butyl-2-(4-fluoro-3-methyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

4-(8-Butyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-benzenesulfonamide;

8-Butyl-2-(3-fluoro-4-methoxy-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

N-[5-(8-Butyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-2-cyano-phenyl]-acetamide;

8-Butyl-2-(3-methoxy-5-trifluoromethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Butyl-2-(3,4-difluoro-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Butyl-2-(3-chloro-4-iodo-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Butyl-2-(3,5-dimethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Butyl-2-(3-chloro-4-methyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Butyl-2-(4-chloro-3-trifluoromethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

3-(8-Butyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-benzenesulfonamide;

8-Butyl-2-(5-oxo-5,6,7,8-tetrahydro-naphthalen-2-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Butyl-2-(3,5-difluoro-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

N-[5-(8-Butyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-2-methyl-phenyl]-methanesulfonamide;

8-Isopropyl-2-(3-nitro-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(4-Fluoro-3-trifluoromethyl-phenylamino)-8-isopropyl-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(4-Fluoro-3-methyl-phenylamino)-8-isopropyl-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(1H-Indol-5-ylamino)-8-isopropyl-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(1H-Benzotriazol-5-ylamino)-8-isopropyl-8H-pyrido[2,3-d]pyrimidin-7-one;

[4-(8-Isopropyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-phenyl]-carbamic acid tert-butyl ester;

2-(3,5-Dichloro-4-hydroxy-phenylamino)-8-isopropyl-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(3-Chloro-4-hydroxy-phenylamino)-8-isopropyl-8H-pyrido[2,3-d]pyrimidin-7-one;

N-[4-(8-Isopropyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-phenyl]-acetamide;

8-Butyl-2-(2-fluoro-5-nitro-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(4-Chloro-3-methyl-phenylamino)-8-isopropyl-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Isopropyl-2-(3,4,5-trimethoxy-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

4-(8-Isopropyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-benzenesulfonamide;

2-(3-Chloro-4-fluoro-phenylamino)-8-isopropyl-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(2-Fluoro-5-nitro-phenylamino)-8-isopropyl-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(4-Chloro-3-trifluoromethyl-phenylamino)-8-isopropyl-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(3-Fluoro-4-methoxy-phenylamino)-8-isopropyl-8H-pyrido[2,3-d]pyrimidin-7-one;

4-(8-Isopropyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-phthalonitrile;

N-[2-Cyano-5-(8-isopropyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-phenyl]-acetamide;

8-Isopropyl-2-(3-methoxy-5-trifluoromethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(3,4-Difluoro-phenylamino)-8-isopropyl-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(3-Iodo-4-methyl-phenylamino)-8-isopropyl-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(2-Fluoro-5-trifluoromethyl-phenylamino)-8-isopropyl-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(3,5-Dichloro-phenylamino)-8-isopropyl-8H-pyrido[2,3-d]pyrimidin-7-one;

3-(8-Isopropyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-benzenesulfonamide;

8-Isopropyl-2-(5-oxo-5,6,7,8-tetrahydro-naphthalen-2-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

N-[4-(8-Isopropyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-phenyl]-N-methyl-acetamide;

4-(8-Isopropyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-benzonitrile;

2-(3,4-Dimethyl-phenylamino)-8-isopropyl-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(4-Hydroxy-3-methyl-phenylamino)-8-isopropyl-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(4-Hydroxy-3-morpholin-4-ylmethyl-phenylamino)-8-isopropyl-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(2,3-Dihydro-1H-indol-5-ylamino)-8-isopropyl-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(1H-Indazol-6-ylamino)-8-isopropyl-8H-pyrido[2,3-d]pyrimidin-7-one;

N-[5-(8-Isopropyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-2-methyl-phenyl]-methanesulfonamide;

N-[5-(8-Isopropyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-2-methyl-phenyl]-acetamide;

2-(4-Hydroxy-3,5-dimethyl-phenylamino)-8-isopropyl-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(4-Bromo-3-methyl-phenylamino)-8-isopropyl-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Isopropyl-2-(4-trifluoromethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Isopropyl-2-(4-trifluoromethoxy-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

N-[2-Cyano-4-(8-isopropyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-phenyl]-acetamide;

8-sec-Butyl-2-phenylamino-8H-pyrido[2,3-d]pyrimidin-7-one;

8-sec-Butyl-2-(1H-indol-5-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-sec-Butyl-2-(1H-indazol-5-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(1H-Benzotriazol-5-ylamino)-8-sec-butyl-8H-pyrido[2,3-d]pyrimidin-7-one;

[4-(8-sec-Butyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-phenyl]-carbamic acid tert-butyl ester;

8-sec-Butyl-2-(2-fluoro-4-hydroxy-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-sec-Butyl-2-(3-chloro-4-hydroxy-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-sec-Butyl-2-(3-nitro-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-sec-Butyl-2-(3,4-dimethoxy-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-sec-Butyl-2-(4-methoxy-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-sec-Butyl-2-(4-chloro-3-methyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-sec-Butyl-2-(3,4,5-trimethoxy-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-sec-Butyl-2-(4-fluoro-3-trifluoromethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-sec-Butyl-2-(2-fluoro-5-nitro-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-sec-Butyl-2-(3-chloro-4-fluoro-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-sec-Butyl-2-(3,4,5-trichloro-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-sec-Butyl-2-(3-fluoro-4-methoxy-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-sec-Butyl-2-(3-methoxy-5-trifluoromethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-sec-Butyl-2-(3-chloro-4-iodo-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-sec-Butyl-2-(3-iodo-4-methyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-sec-Butyl-2-(2-fluoro-5-trifluoromethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-sec-Butyl-2-(3-chloro-4-methyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-sec-Butyl-2-(4-chloro-3-trifluoromethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

3-(8-sec-Butyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-benzenesulfonamide;

8-sec-Butyl-2-(5-oxo-5,6,7,8-tetrahydro-naphthalen-2-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

N-[4-(8-sec-Butyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-phenyl]-N-methyl-acetamide;

8-sec-Butyl-2-(3,5-difluoro-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Cyclopentyl-2-(2,4,6-trifluoro-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

4-(8-sec-Butyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-benzonitrile;

8-sec-Butyl-2-(4-fluoro-3-nitro-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-sec-Butyl-2-(3,4-dimethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-sec-Butyl-2-(3-trifluoromethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(3-Bromo-4-methyl-phenylamino)-8-sec-butyl-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(4-Bromo-3-methyl-phenylamino)-8-sec-butyl-8H-pyrido[2,3-d]pyrimidin-7-one;

N-[5-(8-sec-Butyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-2-methyl-phenyl]-methanesulfonamide;

2-(3-Chloro-4-fluoro-phenylamino)-8-(1-ethyl-propyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1-Ethyl-propyl)-2-(3-fluoro-4-methyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(2,4-Difluoro-phenylamino)-8-(1-ethyl-propyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

4-[8-(1-Ethyl-propyl)-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino]-benzonitrile;

8-(1-Ethyl-propyl)-2-(3-trifluoromethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(4-Chloro-3-trifluoromethyl-phenylamino)-8-(1-ethyl-propyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1-Ethyl-propyl)-2-(3-trifluoromethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(4-Bromo-3-trifluoromethyl-phenylamino)-8-(1-ethyl-propyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1-Ethyl-propyl)-2-(3-nitro-4-trifluoromethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1-Ethyl-propyl)-2-(3-iodo-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(3,4-Dimethyl-phenylamino)-8-(1-ethyl-propyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1-Ethyl-propyl)-2-(1H-indol-5-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1-Ethyl-propyl)-2-(2-oxo-2,3-dihydro-1H-benzimidazol-5-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

{4-[8-(1-Ethyl-propyl)-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino]-phenyl}-carbamic acid tert-butyl ester;

8-(1-Ethyl-propyl)-2-(2-fluoro-4-hydroxy-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(3-Chloro-4-hydroxy-phenylamino)-8-(1-ethyl-propyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(3,5-Dichloro-4-hydroxy-phenylamino)-8-(1-ethyl-propyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1-Ethyl-propyl)-2-(3-nitro-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(3,4-Dimethoxy-phenylamino)-8-(1-ethyl-propyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(4-Chloro-3-methyl-phenylamino)-8-(1-ethyl-propyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1-Ethyl-propyl)-2-(3,4,5-trimethoxy-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1-Ethyl-propyl)-2-(4-fluoro-3-trifluoromethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1-Ethyl-propyl)-2-(4-fluoro-3-methyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1-Ethyl-propyl)-2-(2-fluoro-5-nitro-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1-Ethyl-propyl)-2-(3-fluoro-4-methoxy-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

N-{2-Cyano-5-[8-(1-ethyl-propyl)-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino]-phenyl}-acetamide;

2-(4-Bromo-3-chloro-phenylamino)-8-(1-ethyl-propyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1-Ethyl-propyl)-2-(3-methoxy-5-trifluoromethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(3,4-Difluoro-phenylamino)-8-(1-ethyl-propyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(3,5-Difluoro-phenylamino)-8-(1-ethyl-propyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(3,4-Dichloro-phenylamino)-8-(1-ethyl-propyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1-Ethyl-propyl)-2-(3-hydroxy-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

N-{4-[8-(1-Ethyl-propyl)-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino]-2-methyl-phenyl}-acetamide;

N-{2-Chloro-4-[8-(1-ethyl-propyl)-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino]-6-fluoro-phenyl}-acetamide;

8-(1-Ethyl-propyl)-2-(4-trifluoromethoxy-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(9H-Carbazol-3-ylamino)-8-(1-ethyl-propyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1-Ethyl-propyl)-2-(2-oxo-2,3-dihydro-benzoxazol-5-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1-Ethyl-propyl)-2-(1H-indazol-6-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

N-{5-[8-(1-Ethyl-propyl)-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino]-2-methyl-phenyl}-methanesulfonamide;

8-(1-Ethyl-propyl)-2-(3-oxo-3,4-dihydro-2H-1,4-benzothiazin-6-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(4-Amino-3,5-dichloro-phenylamino)-8-(1-ethyl-propyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

N-{5-[8-(1-Ethyl-propyl)-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino]-2-methyl-phenyl}-acetamide;

8-(1-Ethyl-propyl)-2-(4-hydroxy-3,5-dimethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

5-[8-(1-Ethyl-propyl)-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino]-2-hydroxy-benzoic acid;

8-(1-Ethyl-propyl)-2-(indan-5-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(1-Ethyl-propyl)-2-(4-trifluoromethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(4-Bromo-3-methyl-phenylamino)-8-(1-ethyl-propyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Cyclopentyl-2-(1H-indol-5-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Cyclopentyl-2-(1H-indazol-6-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Cyclopentyl-2-(3-trifluoromethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

4-(8-Cyclopentyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-benzonitrile;

8-Cyclopentyl-2-(3,4-dichloro-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Cyclopentyl-2-(4-trifluoromethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Cyclopentyl-2-(4-fluoro-3-trifluoromethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

[4-(8-Cyclopentyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-phenyl]-carbamic acid tert-butyl ester;

8-Cyclopentyl-2-(1H-indazol-5-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(1H-Benzotriazol-5-ylamino)-8-cyclopentyl-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Cyclopentyl-2-(2-fluoro-4-hydroxy-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(3-Chloro-4-hydroxy-phenylamino)-8-cyclopentyl-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Cyclopentyl-2-(3,5-dichloro-4-hydroxy-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Cyclopentyl-2-(3,4-dimethoxy-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Cyclopentyl-2-(3-fluoro-4-methoxy-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Cyclopentyl-2-(3-methoxy-5-trifluoromethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Cyclopentyl-2-(3,5-dimethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(3-Chloro-4-methyl-phenylamino)-8-cyclopentyl-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(4-Chloro-3-trifluoromethyl-phenylamino)-8-cyclopentyl-8H-pyrido[2,3-d]pyrimidin-7-one;

3-(8-Cyclopentyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-benzenesulfonamide;

8-Cyclopentyl-2-(3,5-difluoro-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Cyclopentyl-2-(3,4-dimethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Cyclopentyl-2-(4-hydroxy-3-morpholin-4-ylmethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Cyclopentyl-2-(4-hydroxy-3-nitro-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Cyclopentyl-2-(2,3-dimethyl-2,3-dihydro-1H-indol-5-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Cyclopentyl-2-(2,3-dihydro-1H-indol-5-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Cyclopentyl-2-(2-oxo-2,3-dihydro-benzoxazol-5-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

N-[5-(8-Cyclopentyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-2-methyl-phenyl]-methanesulfonamide;

8-Cyclopentyl-2-(3-oxo-3,4-dihydro-2H-1,4-benzothiazin-6-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(4-Amino-3,5-dichloro-phenylamino)-8-cyclopentyl-8H-pyrido[2,3-d]pyrimidin-7-one;

N-[5-(8-Cyclopentyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-2-methyl-phenyl]-acetamide;

8-Cyclopentyl-2-(4-hydroxy-3,5-dimethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

5-(8-Cyclopentyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-2-hydroxy-benzoic acid;

2-(4-Bromo-3-trifluoromethyl-phenylamino)-8-cyclopentyl-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(4-Bromo-3-methyl-phenylamino)-8-cyclopentyl-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Cyclopropylmethyl-2-(1H-indol-5-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(1H-Benzotriazol-5-ylamino)-8-cyclopropylmethyl-8H-pyrido[2,3-d]pyrimidin-7-one;

[4-(8-Cyclopropylmethyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-phenyl]-carbamic acid tert-butyl ester;

8-Cyclopropylmethyl-2-(2-fluoro-4-hydroxy-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(3-Chloro-4-hydroxy-phenylamino)-8-cyclopropylmethyl-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Cyclopropylmethyl-2-(3,5-dichloro-4-hydroxy-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Cyclopropylmethyl-2-(3,4,5-trimethoxy-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Cyclopropylmethyl-2-(4-fluoro-3-trifluoromethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

4-(8-Cyclopropylmethyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-benzenesulfonamide;

8-Cyclopropylmethyl-2-(2-fluoro-5-nitro-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(3-Chloro-4-iodo-phenylamino)-8-propyl-8H-pyrido[2,3-d]pyrimidin-7-one;

N-[2-Cyano-5-(8-cyclopropylmethyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-phenyl]-acetamide;

8-Cyclopropylmethyl-2-(3,5-difluoro-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Cyclopropylmethyl-2-(4-fluoro-3-nitro-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Cyclopropylmethyl-2-(2-oxo-2,3-dihydro-1H-benzimidazol-5-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Cyclopropylmethyl-2-(3-hydroxy-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

N-[2-Chloro-4-(8-cyclopropylmethyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-6-fluoro-phenyl]-acetamide;

8-Cyclopropylmethyl-2-(2,3-dimethyl-2,3-dihydro-1H-indol-5-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Cyclopropylmethyl-2-(2,3-dihydro-1H-indol-5-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(9H-Carbazol-3-ylamino)-8-cyclopropylmethyl-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Cyclopropylmethyl-2-(1H-indazol-6-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Cyclopropylmethyl-2-(3-oxo-3,4-dihydro-2H-1,4-benzothiazin-6-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

N-[5-(8-Cyclopropylmethyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-2-methyl-phenyl]-acetamide;

8-Cyclopropylmethyl-2-(4-hydroxy-3,5-dimethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Cyclopropylmethyl-2-(indan-5-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Cyclopropylmethyl-2-(3,4,5-trifluoro-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(4-Bromo-3-trifluoromethyl-phenylamino)-8-cyclopropylmethyl-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Cyclopropylmethyl-2-(4-trifluoromethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Cyclopropylmethyl-2-(4-trifluoromethoxy-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

N-[5-(8-Cyclopropylmethyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-2-methyl-phenyl]-methanesulfonamide;

2-(1H-Indol-5-ylamino)-8-(2,2,2-trifluoro-ethyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(1H-Indazol-5-ylamino)-8-(2,2,2-trifluoro-ethyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(1H-Benzotriazol-5-ylamino)-8-(2,2,2-trifluoro-ethyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(2-Fluoro-4-hydroxy-phenylamino)-8-(2,2,2-trifluoro-ethyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(3-Chloro-4-hydroxy-phenylamino)-8-(2,2,2-trifluoro-ethyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(3,5-Dichloro-4-hydroxy-phenylamino)-8-(2,2,2-trifluoro-ethyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(3-Nitro-phenylamino)-8-(2,2,2-trifluoro-ethyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(3,4-Dimethoxy-phenylamino)-8-(2,2,2-trifluoro-ethyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-Phenylamino-8-(2,2,2-trifluoro-ethyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(3-Fluoro-4-methoxy-phenylamino)-8-(2,2,2-trifluoro-ethyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

4-[7-Oxo-8-(2,2,2-trifluoro-ethyl)-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino]-phthalonitrile;

N-{2-Cyano-5-[7-oxo-8-(2,2,2-trifluoro-ethyl)-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino]-phenyl}-acetamide;

2-(4-Bromo-3-chloro-phenylamino)-8-(2,2,2-trifluoro-ethyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(3-Methoxy-5-trifluoromethyl-phenylamino)-8-(2,2,2-trifluoro-ethyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(3,4-Difluoro-phenylamino)-8-(2,2,2-trifluoro-ethyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(2,2,2-Trifluoro-ethyl)-2-(2,4,6-trifluoro-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(3,5-Difluoro-phenylamino)-8-(2,2,2-trifluoro-ethyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(4-Fluoro-3-nitro-phenylamino)-8-(2,2,2-trifluoro-ethyl)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-(2,2,2-Trifluoro-ethyl)-2-(3-trifluoromethyl-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

N-{2-Methyl-4-[7-oxo-8-(2,2,2-trifluoro-ethyl)-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino]-phenyl}-acetamide;

8-Cyclohexyl-2-(3,4-dimethoxy-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(1H-Indol-5-ylamino)-8-methyl-8H-pyrido[2,3-d]pyrimidin-7-one;

[4-(8-Methyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-phenyl]-carbamic acid tert-butyl ester;

2-(3-Chloro-4-hydroxy-phenylamino)-8-methyl-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(3,4-Dimethoxy-phenylamino)-8-methyl-8H-pyrido[2,3-d]pyrimidin-7-one;

2-(2-Fluoro-5-nitro-phenylamino)-8-methyl-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Methyl-2-(3,4,5-trimethoxy-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

4-(8-Methyl-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidin-2-ylamino)-2-trifluoromethyl-benzonitrile;

8-Ethyl-2-(1H-indol-5-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Isopropyl-2-(4-methoxy-phenylamino)-8H-pyrido[2,3-d]pyrimidin-7-one;

8-Isopropyl-2-(3-nitro-phenylamino)-8*H*-pyrido[2,3-*d*]pyrimidin-7-one; and

8-Isopropyl-2-(4-hydroxy-phenylamino)-8*H*-pyrido[2,3-*d*]pyrimidin-7-one.

13. A method for treating a mammal suffering from a neurodegenerative disease and in need of treatment comprising administering an effective amount of a compound of Claim 12.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 00/32572

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07D471/04 A61K31/505 A61P25/28 //(C07D471/04,239:00, 221:00)

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07D A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, BEILSTEIN Data, WPI Data, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 33798 A (DOHERTY ANNETTE MARIAN ;DOBRUSIN ELLEN MYRA (US); WARNER LAMBERT C) 6 August 1998 (1998-08-06) cited in the application see examples	12
X	WO 97 20842 A (CENTRE NAT RECH SCIENT ;MEIJER LAURENT (FR); BISAGNI EMILE (FR); L) 12 June 1997 (1997-06-12) page 11	1,2,9-11
X	ALVAREZ ET AL.: "Inhibition of tau phosphorylating protein..." FEBS LETTERS, vol. 459, 1999, pages 421-426, XP002163858 page 425	1,2,9-11

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

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"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
26 March 2001	09/04/2001

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Steendijk, M

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 00/32572

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
A	PATRICK GENTRY N ET AL: "Conversion of p35 to p25 deregulates Cdk5 activity and promotes neurodegeneration" NATURE,GB,MACMILLAN JOURNALS LTD. LONDON, vol. 402, no. 6762, 9 December 1999 (1999-12-09), pages 615-622, XP002136732 ISSN: 0028-0836 the whole document	1-12

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/US 00/32572

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		BR 9807305 A	02-05-2000
		EP 0964864 A	22-12-1999
		HR 980060 A	30-06-1999
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		EP 0874847 A	04-11-1998
		JP 2000501408 T	08-02-2000